PREVALENCE AND CLINICAL OUTCOME OF ANTENATALLY DIAGNOSED RENAL ANOMALIES

Dissertation Submitted

by

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In partial fulfillment of the requirements for the degree of doctor of Medicine (M.D) in Paediatrics

THE TAMILNADU DR.MGR UNIVERSITY

DEPARTMENT OF PAEDIATRICS

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TAMILNADU, INDIA

APRIL – 2017

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To
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Ref: Project No:14/435

Date: February 18, 2015

Dear Dr Thiyagarajan,

Institutional Human Ethics Committee, PSG IMS&R reviewed and discussed your application dated 12.12.2014 to conduct the research study entitled *"Prevalence and clinical outcome of antenatally diagnosed renal anomalies"* during the IHEC meeting held on 08.01.2015.

The following documents were reviewed and approved:

1. Project Submission form
2. Study protocol
3. Parental consent form
4. Permission letter from concerned Heads of the Department
5. Current CVs of Principal Investigator, Co-investigators
6. Budget

The following members of the Institutional Human Ethics Committee (IHEC) were present at the meeting held on 08.01.2015 at IHEC Secretariat, PSG IMS & R between 10.00 am and 11.00 am:

Sl. No.	Name of the Member of IHEC	Qualification	Area of Expertise	Gender	Affiliation to the Institution Yes/No	Present at the meeting Yes/No
1	Dr. P. Sathyan (Chairperson, IHEC)	DO, DNB	Clinician (Ophthalmology)	Male	No	Yes
2	Dr. S. Bhuvaneshwari (Member-Secretary, IHEC)	MI	Clinical Pharmacology	Female	Yes	Yes
3	Dr. S Shanthakumari	M	Pathology, Ethicist	Female	Yes	Yes
4	Dr. D. Vijaya	M Sc, Ph D	Basic Medical Sciences (Biochemistry)	Female	Yes	Yes

The study is approved in its pre sented form. The decision was arrived at through consensus. Neither PI nor any of proposed study team memb s were present during the decision making of the IHEC. The IHEC functions in accordance with the ICH-GCP/IC R/Schedule Y guidelines. The approval is valid until one year from the date of sanction. You may make a written equest for renewal / extension of the validity, along with the submission of status report as decided by the IHEC.

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Following points must be noted:

1. IHEC should be informed of the date of initiation of the study
2. Status report of the study should be submitted to the IHEC every 12 months
3. PI and other investigators should co-operate fully with IHEC, who will monitor the trial from time to time
4. At the time of PI's retirement/intention to leave the institute, study responsibility should be transferred to a colleague after obtaining clearance from HOD, Status report, including accounts details should be submitted to IHEC and extramural sponsors
5. In case of any new information or any SAE, which could affect any study, must be informed to IHEC and sponsors. The PI should report SAEs occurred for IHEC approved studies within 7 days of the occurrence of the SAE. If the SAE is 'Death', the IHEC Secretariat will receive the SAE reporting form within 24 hours of the occurrence
6. In the event of any protocol amendments, IHEC must be informed and the amendments should be highlighted in clear terms as follows:
   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)
   b. Alteration in the budgetary status should be clearly indicated and the revised budget form should be submitted
   c. If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval
   d. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented
   e. If there are any amendments in the trial design, these must be incorporated in the protocol, and other study documents. These revised documents should be submitted for approval of the IHEC and only then can they be implemented
   f. Any deviation-Violation/waiver in the protocol must be informed to the IHEC within the stipulated period for review
7. Final report along with summary of findings and presentations/publications if any on closure of the study should be submitted to IHEC

Kindly note this approval is subject to ratification in the forthcoming full board review meeting of the IHEC.

Thanking You,

Yours Sincerely,

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INSTITUTIONAL HUMAN ETHICS COMMITTEE

Dr S Bhuvaneshwari
Member - Secretary
Institutional Human Ethics Committee

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PREVALENCE AND CLINICAL OUTCOME OF ANTENATALLY DIAGNOSED RENAL ANOMALIES

INTRODUCTION:

The congenital anomalies of kidney andurinary tract (CAKUT) cause morbidity in children (1). The uncertainty in the clinical classification of antenatal detected renal anomalies resulted in the aggregation of different entities under the single label acronym congenital anomalies of kidney and the urinary tract. It is one amongthe leading cause of renal failure in childhood, causing a significant burden in young adults. It account for about 40–50% of children having chronic kidney disease (2). CAKUT constitute about 15-20% of all the antenatally diagnosed congenital anomalies (3).

Antenatally detected urinary tract abnormalities are the most common anomaly detected by antenatal ultrasound. CAKUTs comprise a wide range of renal system structural and functional malformations that occur at the kidney, collecting system , bladder and urethra . These anomalies include absence of kidneys, structural abnormalities in the kidney like multicystic dysplastic kidney, hydronephrosis,ureteric dilatation, vesicoureteral reflux , pelvic ureter junction obstructionand posterior urethral valves. (2)

Ultrasound scans done during the pregnancy has resulted in increased detection of CAKUT. With improved prenatal screening, many cases of CAKUT are diagnosed by antenatal ultrasonography performed during 18–20

weeks of gestation. Before prenatal ultrasound became widely available, children with hydronephrosis often presented with associated symptoms such as infection, pain, hematuria , or palpable mass and surgical intervention was the primary role for alleviation of these symptoms. The use of antenatal ultrasound routinely has led to earlier diagnosis of the asymptomatic patient with an associated shift in treatment to renal preservation rather than symptomatic relief.

The antenatal detected anomalies causes anxiety in parents. They should be counselled for the follow up during postnatal period. Once diagnosed as CAKUT, the parents need to be counselled regarding the outcome of the anomalies. Early antenatal diagnosis is important for counselling the parents for possible intervention and for delivering in the appropriate centre and for further evaluation of the baby. The significance of prenatal diagnosis helps to detect those having anomalies and counsel them. The early evaluation in postnatal period and treatment should started to reduce the adverse outcomes. The risk also should be explained to the parents during counselling.The degree of dilatation of the urinary tract does not always correlate with prognosis. The dilatation of the urinary tract is a dynamic process, which not only can vary over time, but is also influenced by other factors.

The normal urinary tract in ultrasound is better visualised from 9 to 12 weeks of gestational age. During the first trimester kidneys are relatively hyperechogenic in ultrasound. The cortico-medullary differentiation begins by

15 weeks. The renal echogenicity decreases than the echogenicity of liver and spleen by 17 weeks of gestational age . The renal cortex and renal medulla can be clearly distinguished by their hyperechogenic and hypoechogenic respectively at end of 20 weeks of gestation.

The features noted to be documented in ultrasound scan is to locate the both the kidneys, size of the kidneys and the site of location of the kidneys. The USG helps in knowing the structural abnormalities in the kidney and its echogenicity. The bladder is also examined for its size and shape. Amniotic fluid is measured in ultrasound scan. The development of external genitalia also should be looked for. The urine production in the foetus starts around 9 weeks of gestational age. The urine production increases significantly after 16 weeks of gestation. The fetal urine constitutes about 90% of the amniotic fluid around 20 weeks of gestation. The deepest pocket of the amnioticfluid sac is used to measure the amniotic fluid index. It is an objective measurement. (5).

Current trend directs the cause for CAKUT could be due to genes defects. CAKUT when associated with other organ anomalies, syndromicassociation should be considered. They are that are due togene mutations involved in development of kidney. The proteins are involved in the development is altered, so the process can result from normal kidneys with good function to severe renal problems even renal failcure occurs. The evaluation for CAKUT should include evaluation the cause of the disease,

detailed historyincluding family history , investigation and treatment. Genetic counselling also should be offered to the parents.

CAKUT is increased in mothers who have diseases like diabetes mellitus, hyothyroidism and renal disease. It should be discussed in prenatal counseling and management of women with these risk factors (11).

REVIEW OF LITERATURE

Development of kidney :

The kidneys are developed from the intermediate mesoderm. Urinary bladder and urethra develop from the urogenital sinus.The development of the urinary tract begins around 3 weeks of gestation. Ureter arises from mesoderm. The collecting part of the kidney is derived from the diverticulum called the ureteric bud. Kidney development has three stages: Pronephros, Mesonephros and Metanephros. Pronephros&mesonephros are transitory while metanephros develops into the permanent kidney (5).

The pronephros is formed in relation to the nephrogeniccord . It is the primitive excretion system developed at 4 week of intrauterine life. The mesonephros develops in the thoracolumbar region and metanephros from the metanephros from the sacral region. In humans the pronephros is non-functional. Pronephros gets disappeared at 5^{th} week of intrauterine life except for its caudal part. The mesonephric duct also known as wolffian duct is formed around 25^{th} day of gestatioan age. The caudal portion of pronephric duct interacts with the mesenchyme and lead to formation of mesonephros. Most of themesonephric tubules disappear but few in males develop into testicular efferent ducts. But in the females all of them get atrophied.

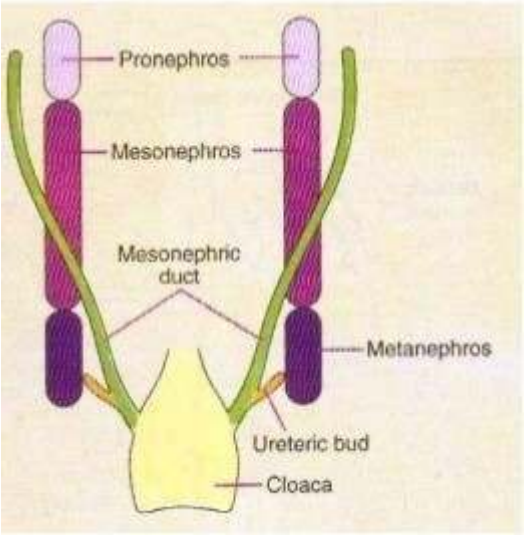


Fig 1 : Pronephros , Mesonephros and Metanephros

The permanent kidney develops from the three intermediate mesoderm structures of the sacral region. They constitutes of ureteric bud, the metanephricblastema and the glomerular capillary network. The ureteric bud is derived from the mesonephric duct duringfifth week gestation and it invades themetanephricblastema..Signals fromureteric bud interact with the mesenchymal cellsand differentiate into the different cell types of the glomerulus and the proximal tubules, distal tubules and loop of henle. The ureteric bud branching is essential in the development of the number of glomeruli or nephrons. At birth, each kidney contains about 1 million nephrons. The nephron maturation begins around 7^{th} week of gestation.Collecting system gets developed by 20 weeks of gestational age contains approximately 30 % of nephrons. Development of nephrons gets completed at around 34^{th} week of gestational age . The functional maturation continues for atleast till six months after birth (4). The defects in any signal activities will cause damage in the

developing kidney. It will lead to conditions like agenesis of kidneys (absence),dysgenesis (abnormal differentiation). The dysgenesis includes aplasia , cystic disease and dysplasia of kidneys.

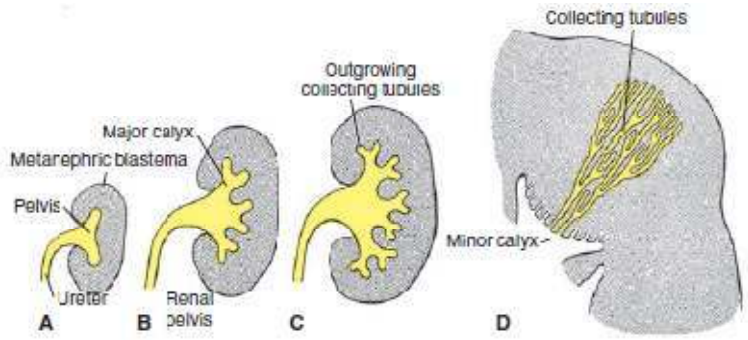


Fig 2: Development of the renal pelvis, calyces, and collecting tubules of the metanephros. A. 6 weeks. B. At end of the 6th week. C. 7 weeks. D. Newborn

The upper urinary tract is derived from the ureteric bud. It comprises of bladder neck, ureter, pelvic calyceal system and nephroncalled the ductuscolligens. Urogenital sinus gives rise to lower urinary tract. It is an endodermal derivate. The upper part of it gives rise to the urinary bladder and the lower part develops into urethra. The tail end of the mesonephric duct and the ureter is absorbed into urogenital sinus. The cranio-caudal exchange of the position of these two structures leads to formation of triangular -zone called the bladder trigonum. The internalmale sex derived from the mesonephric duct and while it getsatrophiedin females.During the embryo development, the differential growth of the abdominal wall causes kidney to ascend to the lumbar region.

The common antenatal manifestations of CAKUT in antenatal period include oligohydraminos , variations in morphology of kidneys , ureter and bladder. After birth, CAKUT can be manifested as palpable abdominal pass , decreased urine output , feeding difficulties and with symptoms of urinary tract infections. CAKUT can develop in association with syndromes, but most cases are non syndromic. SyndromicCAKUTs occur with additional involvement of other organs. Few studies have been done on genetic association in development on cakut. The studies on mice model implicates that nonsyndromic human CAKUT may be caused by single-gene defects (2,6). HNF 1B and PAX2 are the most common genes implicated to cause CAKUT. Other cases may be sporadic as a result of many rare genes causing these disease (2).

Abnormalities in development of kidney and urinary tract :

CAKUT includes multiple conditions that cause the disease due to defects in the origin and development of the kidney and urinary tract. The abnormalities occur due to alterations in the size and/or position of the kidneys, in numbers , dilatation of urinary tract either due to obstructive or non-obstructive causes and dysplastic kidney including cystic disorders. The spectrum of diseases encompassed by the term "CAKUT" is wide. They are**:**

1.Fetal kidney anomalies (renal malformations)

- Renal agenesis (renal aplasia)
- Multicystic dysplastic kidneys
- Renal hypoplasia

2.Fetal ureteric anomalies

- Megaureter.
- Ureteropelvic junction obstruction (PUJO).
- Ureterovesical junction obstruction (UVJO).
- Duplex kidneys/ureters (renal duplications).
- Incompetence of UVJ.

3.Fetal vesical anomalies (anomalies of the bladder)

4.Fetal urethral anomalies

Etiology of urinary tract dilatation detected on antenatal ultrasound (7)	
Etiology	**Incidence (%)**
Transient/physiologic hydronephrosis	50-70
Pelviureteric junction obstruction	10-30
Vesicoureteric reflux	10-40
Vesicoureteric junction obstruction, megaureter	5-15
Multicystic dysplastic kidney	2-5
Posterior urethral valves	1-5
Duplex kidneys (±ureterocele), ectopic ureter, urethral atresia, urogenital sinus, prune belly syndrome, tumors	Uncommon

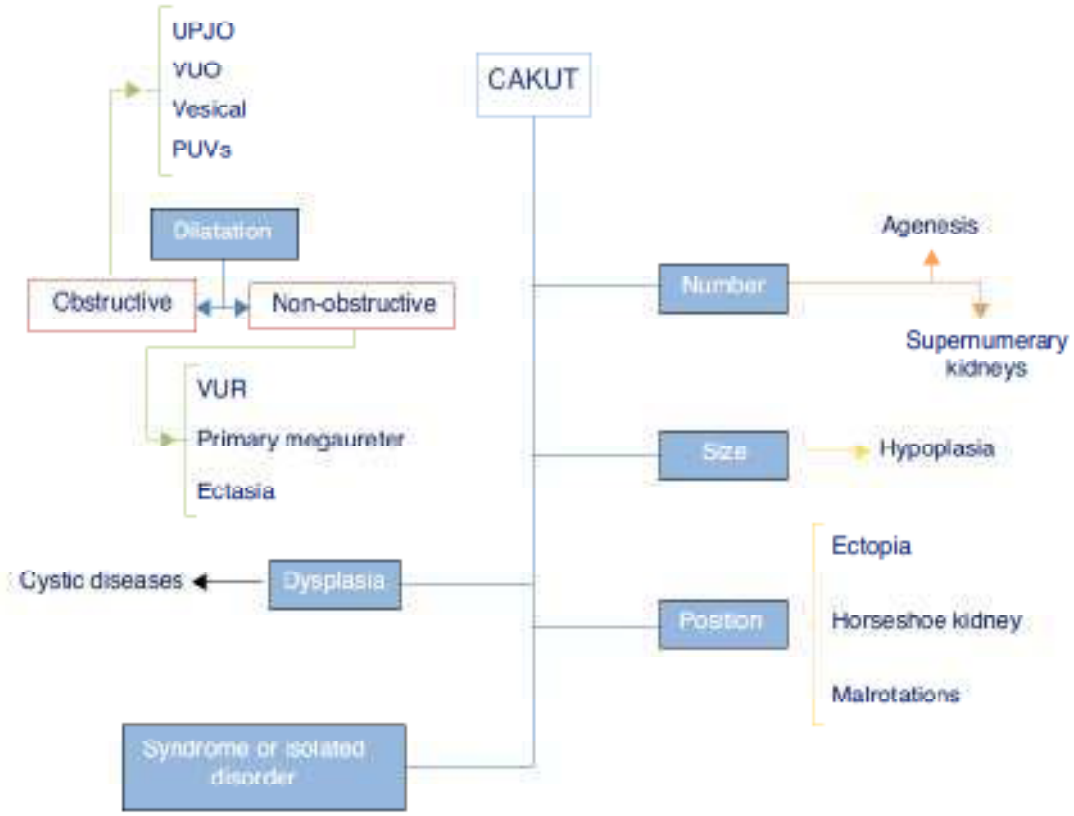


Fig:3. Flowchart diagram showing various causes of CAKUT(12).

Due to confusion associated with terminologies for urinary tract dilatation, the consensus panel recommended avoiding the non specific terminologies for describing urinary tract dilatation likepyelectasis, pelviectasis, ureteronephrosis, UT fullness or prominence, and pelvic fullness.The panel recommend the consistent use of term "UT dilatation" (9). The classification UT dilatation is further based on sonographic findings.

Hydronephrosis :

Hydronephrosis is the most common identified renal anomaly (dicke et al, 2006). The obstruction to urine resulting in dilatation of the renal pelvis and calyces is hydronephrosis(9). It literally means “water in the kidney”. Antenatal hydronephrosis is associated with vesicoureteral reflux or urinary tract obstruction in 14–21% of cases. (10). The majority of the hydronephrosis were isolated. The dilation of urinary tract in antenatal detected hydronephrosis is due to large volume of fetal urine.The kidneys of foetus have smallrole in maintenance homeostasis of salt and water. Urine production increases throughout the gestational age. At 37 weeks the urine volume is reported to be about 50 ml/hour. GFR triples by 3 months of age.The circulatory and the hormonal changes soon after birth leads to decrease in urine output. It results in the resolution of the antenatal detected hyronephrosis and ureter dilation. Some small kinks in ureter causing hydronephrosis also may get resolved over time. Most of the dilation detected in the fetus gets normalized soon after birth and only small percentage of patients will have severe obstruction and end up with surgery (13).

Renal agenesis :

The absence ofdevelopment of kidney is termed as renal agenesis. It can occur due to defect in the mesonephric duct,metanephricblastema and ureteric bud. The incidence of agenesis of single kidney is 1 in 1000 live births .cascio et al in his study mentioned the prevalence to be 1 in 1300. Bilateral

agenesis is a lethal condition , a rare entity seen nowadays. The unilateral absent kidney is mostly isolated. It can also be a part of syndromic association. It can be associated with part of VACTERL anomalies.

“VACTERL” anomalies should be considered, if it has at least 3 of the following congenital malformations:

- Vertebral defects – (hemivertebrae, fused vertebrae)
- Anal atresia or imperforate anus
- Cardiac defects – VSD is common
- TEF - Tracheo-esophageal fistula
- Renal anomalies(renal agenesis) and
- Limb abnormalities(radial agenesis, thumb hypoplasia).

True agenesis involves the ipsilateral absence of ureter, and ipsilateral bladder trigone. On USG investigation ther is emptiness in lumbar fossa and the adrenal gland appears enlarged. It classically denotes “lying down adrenal sign”. In individuals with single functioning kidney are attributed to increased risk of chronic kidney disease in adulthood (4, 14,15).

The contralateral kidney undergoes compensatory hypertrophy before birth but most of them ocuurs after birth. 15 % of children with agenesis of single kidney tend to havevesicoureteral reflux in opposite kidney. Since the wolffian duct is absent, the vas deferens is absent in the same side of absent kidney. Mullerian duct abnormalities are common in girls. It is due to the contiguous nature of both mullerian ducts and wolffian ducts. The findings that

includes absence of kidneys in same side or located in abnormal position on same side, mulleriandefectson same side and absence of vagina refers to a syndrome called Mayer RokitanskyKusterHauser (MRKH) syndrome.

Bilateral renal agenesis is life threatening, with 50% fetuses are stillborn and the rest would die shortly after birth. It occurs in contion potter syndrome. The characteristic features are typical facial appearance, termed potter facies comprises widely separated eyes, low set ears, flat nose, redundant and dehydrated skin , receding chin and limb anomalies. It has prevalence of 1 in 3000 pregnancies.

The ultrasound findings of bilateral renal agenesis are (16):

- Non -visualization of both the kidneys in bilateral renal fossae, as well as in the entire abdominal cavity,
- Lying down adrenal sign,
- Renal fossae occupied by the bowel gas in late 3rd trimester,
- Severe oligohydramnios,
- Nonvisualization of urinary bladder,
- Pulmonary hypoplasia,
- Associated other congenital anomalies.

ARPKD – infantile type , cystic kidney disease, renal hypoplasia and dysplasia of medulla are the other causes of renal failure in neonates with potter syndrome. The babies born with absence of both kidneys will die of pulmonary failure due to hypoplasia of lungs rather than renal failure(4).

Figure 4. USG of fetal abdomen shows that both the renal fossae are not occupied by kidneys, and are occupied by the adrenal glands producing low lying adrenal sign.

Fig 5: CXR showing bell-shaped thorax, suggestive of pulmonary hypoplasia

Fig 6: Potter facies

Ectopic kidney :

The prevalence of ectopic kidneys is about 1 in 1000 pregnancies. During renal embryogenesis it normally ascends from the pelvis into lumbar region. Renal ectopia occurs when the process of ascending from sacral to lumbar region is incomplete. Ectopic kidneyis seen in pelvis , iliac region, thoracic region and contralateral position. The kidneys get fused when the ectopia is bilateral. Fusion is more common in lower pole resulting in horseshoe kidney. Horseshoe kineys is more prevalent in turner syndrome. The incidence of wilms tumour in children with horse shoe kidney is four times more than other children.

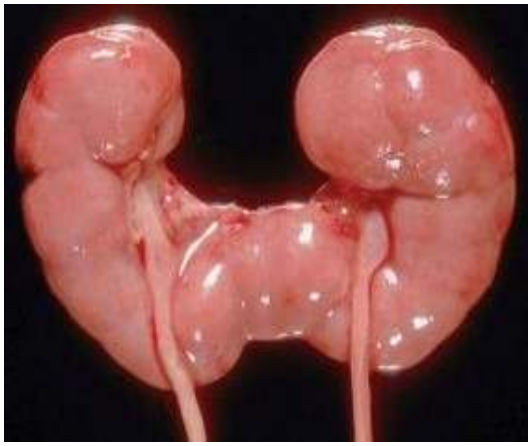


Fig 7 : Horse shoe kidney - both fused in the lower pole

Multicystic dysplastic kidney (MCDK):

The developmental malformation of kidney that affect its size, shape or structure is referred as renal dysgenesis. There are three types of dysgenesis : dysplastic , hypoplastic and cystic. Hypoplasia means there is decrease in

number of nephrons, it can occur as isolated condition. The term dysplasia denotes focal , diffuse or segmentally arranged primitive structures resulting in abnormal metanephric differentiation. Other elements apart from renal tissues like cartilages can be seen. MCDK can involve the entire kidney or only a certain part. In a kidney when cysts are developed, it is known as cystic dysplasia**. W**hen the entire kidney is dysplastic with predominance of cysts, it is known asmulticystic dysplastic kidney (4).

The etiology of MCDK is still unclear. Some causes considered are infections, teratogenicdrugs , genetic disturbances and urinary tract obstructions. Mutations in the EYA1, SIX1, and PAX2 genes have been correlated. In a family PAX2 mutation had MCDK(as well as other renal anomalies) affected members that has occurred across three generations. Certain antiepileptic medications, infections such as theenterovirus, cytomegalovirus, and adenovirus have also been considered as contributing factors (18).

Fig 8 : Multicystic dysplastic Kidney (MCDK)

Fig 9 : USG of a MCDK patient

The USG of a Multicystic dysplastic kidney shows multiple cysts , giving a appearance of "bunch of grapes". The DTPA renal scan shows no renal function.In patients with MCDK conservative management approach is routinely practiced in many centres. One reason is, this condition is detected antenatal ultrasound and it can be followed up in the post natal period. Many researchers have found that multicysticdysplastic kidney regress over the time. In a study reserachers have noted complete involution rates vary from 19–74% over 9 months to 10 years. Surgical approach is needed when patients have complications such as urinary tract infections, bleeding , flank pain , hypertension and malignant transformation. In studies done by Nishio et al , they found that ultrasound results of MCDK doesn't necessarily mean the involution has completely occurred. USG cannot detect small remnants from an involute cyst.

In unilateral MCDK , the contralateral kidneys are commonly affected. To evaluvate the kidney function , DMSA and VCUG are usually done. A dimercaptosuccinic acid scan (DMSA) is a nuclear medicine scan that generates tomographic and three-dimensional pictures of the kidneys. It detects the cortical scarring caused by contralateral abnormalities and how the kidneys are functioning. It can be used to distinguish between upper and lower UTI. But DMSA scans are not useful in differentiating contralateral renal abnormalities.

Vesicoureteral reflux causes urine to flow backwards from the bladder into the ureter or even the kidney. It causes pain and also scar the kidney or quite possibly disrupt the function of the kidney . A VCUG is a fluoroscopy exam that determines how the bladder is filled and if reflux occurs (18,19).

The abnormalities that affect the contralateral healthy kidney in MCDK are:

- Vesicoureteral reflux
- UVJ obstruction
- Hydronephrosis
- Ureterocele
- Crossed ectopia
- Echogenic kidney
- PUJ Obstruction

Polycystic kidney disease:

It is an autosomal inherited disorder. It is of two types,autosomal recessive (ARPKD) and autosomal dominant (ADPKD). Both the kidneys are involved. ADPKD is characterized by renal cyst development progressing &cyst enlargement with many extra renal manifestations. ADPKD is caused by mutation in PKD1 and PKD2 genes. PKD1 is located on the chromosome (short arm16p). PKD2 is located on the chromosome 4 (long arm 4q). TheADPKD is diagnosed when both the kidneys are enlarged with large cysts and the affected patient have an history of affected individual in the 1st-degree relative. Multiple hepatic lesions have been associated with it. The ARPKD manifests with mass in the abdomen palpated on both side of flanks during the neonatal or infancy period. There is history of oligohydraminos in antenatal period, respiratory distress at birth due to pulmonary hypoplasia, and history of spontaneous pneumothorax in the newborn period.Mutations in PKHD1 causes ARPKD. There will be no family history of renal cysts in child with ARPKD.Hypertension can develop in a child with this disease. Treatment is mainly supportive for both the conditions. Some experts included this polycystic kidney disease into the CAKUT spectrum. But the approach for this disease and management varies from the CAKUT. But most of the clinical features are not shared by common CAKUT conditions . These patients need a regular treatment and follow up (4,12).

Medullary Nephrocalcinosis :

Nephrocalcinosis is defined as renal calcification, is usually associated with hypercalciuric state. 7–64% of preterm neonates with gestational age less than 32 weeks or birth weight less than 1.5 kg , NC was diagnosed . Etiology of nephrocalcinosisin preterm is due to multiple factors. They include prematurity, LBW babies, severe respiratory disease and in imbalance between the stone-promoting factors & stone inhibiting factors.

Etiology :Nephrocalcinosis in preterm:

- Hypercalciuria
- High intake of calcium
- Low phosphorus
- Total Parenteral nutrition
- Diuretics - frusemide,
- Vitamin D
- Glucocorticosteroid
- Hyperoxaluria
- Fat malabsorption,
- Others :
    - Male, family history of kidney stones
    - Nephrotoxic medication, eg, Gentamicin.

The diagnosis is made by ultrasound examination. Spontaneous resolution of nephrocalcinosis occurs in 85 % of children by one year of age. (45). Prematurity itself can be associated with elevated B.P., comparatively smaller kidneys, and tubular dysfunctionin distal tubules. Added to it, nephrocalcinosis in preterm neonates can have long-term problems in renal function.The blood pressure andfunctionof kidneys should be followed up regularly for long term in prematurely born children with neonatalnephrocalcinosis.

Obstructive uropathy:

The urinary tract obstruction at the the junction ureteropelvic junction is the commonest cause of uropathy in babies (20).The incidence is one in 1500 births. Renal pelvis dilation will be seen in the ultrasound investigation done for PUJO. The ureter will not be dilated. The ureter will be involved in conditions like megaureter and UVJO. The ultrasound findings does not correlate clinically. The most of the dilatation gets resolved after birth. The fuctional scan is used for those with persisting anomalies. It is taken prior to surgery to take a decision. DTPA or MAG-3 are used. Ransley at al , concluded in his study that infants having renal pelvis APD greater than 20 mm are at increased risk of functional compromise of the kidney. MRI urogram is available now, it tells about the anatomy and the function of the kidneys The indications for surgery include <40% differential function of the hydronephrotic kidney on MAG3 scanning, a >20-mm anterior-posterior

diameter of the renal pelvis, pain, and infection. Pyeloplasty is the gold-standard treatment (20). The ultimate goal of the treatment in PUJO is to improve the renal drainage, maintain the kidney function or improving it and relieving from symptoms.

Posterior uretheral valve (21, 22) **:**

Posterior uretheral valve is also known as congenital obstructing posterior uretheral valve. The m.c.congenital obstructive lesion of urethra is PUV, occurring only in male infants and is associated with morbidities, including urinary tract infection, chronic renal failure, urinary incontinence and even death. Urethral valves arisesfrom the tissues of wolffian duct origin. PUV occurs early in gestation around 5-7 weeks.The incidence is about 1 in 10000-25000 live births (22). The clinical symptoms depends on severity of the obstruction caused by PUV. The fetus will be S.G.A and in USG scan will revealoligohydraminos.

There are 3 types of PUV. Type 1 is the most common type.

Type 1 - Valves representing folds extending inferiorly from the verumontanum to the membranous urethra.

Type 2 - Valves as leaflets radiating from the verumontanum proximally to the bladder neck, and

Type3 - Valves as concentric diaphragms within the prostatic urethra, either above or below the verumontanum.

Radiographic images of PUV :

- In antenatal USG , PUV is considered if there is
  - Marked distention and hypertrophy of the bladder.
  - Hydronephrosis and hydroureter (may or may not be present)
  - Severe oligohydraminos
  - Increased echogenicity of the kidneys
  - Key hole sign due to the distension of both the bladder and the urethra immediately proximal to the valve.

The USG findings are generally not seen before 26 weeks of gestation.

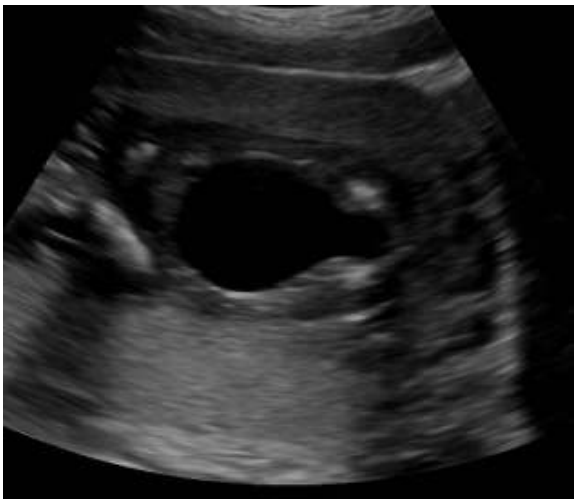


Fig 9 : USG showing keyhole sign

In postnatal scan, the findings are

- Key hole sign - bladder is typically thick-walled and trabeculated with an elongated and dilated posterior urethra.
- Hydronephrosis. In up to 10% of cases kidneys appear normal.
- Hyperechoic kidneys with loss of the normal corticomedullary differentiation.
- Posterior urethra examination ideally performed during micturition. Diameter of more than 6 mm is considered abnormal and is highly specific and sensitive to the diagnosis.
- Valve may be seen as an echogenic line.

In PUV due to the obstruction to urine flow is present , in some patients while voiding high tension is created within the bladder and it may lead to rupture and leads to accumulation of urine in other places.. It includes (1) Calyceal fornix rupture resulting in pararenalurinomas (2) Rupture of bladder intra-peritoneally(accumulated as intraperitoneal fluid, difficult to distinguish in ultrasound from ascites).

VCUGis the imaging of choice for diagnosing the posterior urethral valves. Images taken in the micturition phase gives the better confirmation.

VCUG findings include :

- Dilatation and elongation of the posterior urethra.
- Linear radiolucent band corresponding to the valve
- Vesicoureteric reflux seen in 50% of patients
- Bladder trabeculation or trabecula.

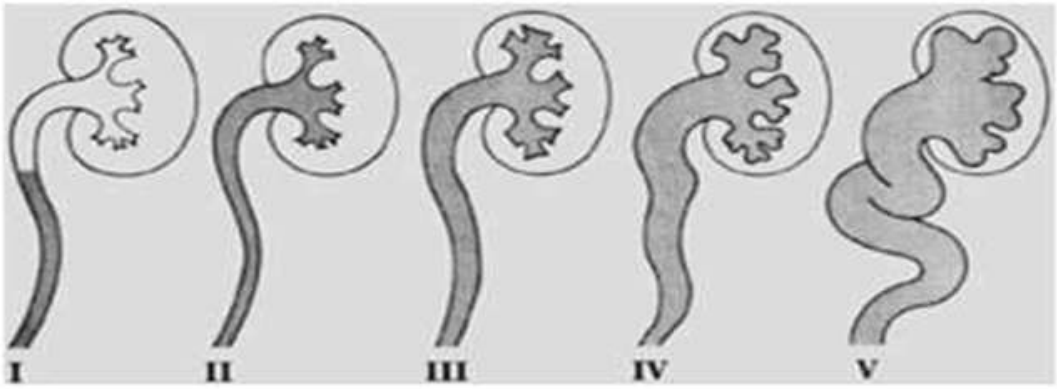
The overall prognosis depends on the degree and duration of obstruction. Antenatal treatment is by doing vesicoamniotic shunting. It allows urine to exit the bladder by the shuntcreated and obstruction to urethra is relieved. This procedure is done by ultrasound guidance and performed in expert hands. After birth the definitive treatment is surgery transurethral ablation (fulgration) of the offending valve.

Vesicoureteralreflux :

The most common uropathy in childhood is VUR (vesicoureteral reflux). It means the retrogradeflow of urine tothe ureter and kidney (upper urinary tract) at rest or while voiding. Primary VUR can either be due to position abnormality in ureterovesical junction (UVJ) or in its integrity. The prevalence of the Vesicoureteral reflux in children is not exactly known, as many of the children are asymptomatic. The prevalence of VUR in children with UTI is 30 % , in infants with posterior uretheral values is 60 % . it is estimated to be 0.4 – 1.8% in normal children.(23)

Classification of Vesicoureteral Reflux

TYPE	CAUSE
Primary	Congenital incompetence of the valvular mechanism of the vesicoureteral junction
Primary associated with other malformations of the ureterovesical junction	Ureteral duplication
	Ureterocele with duplication
	Ureteral ectopia
	Paraureteral diverticula
Secondary to increased intravesical pressure	Neuropathic bladder
	Non-neuropathic bladder dysfunction
	Bladder outlet obstruction
Secondary to inflammatory processes	Severe bacterial cystitis
	Foreign bodies
	Vesical calculi
	Clinical cystitis
Secondary to surgical procedures involving the ureterovesical junction	Surgery



International classification of VUR: (23, 24)

Grading of vesicoureteral reflux (23,24):

- Grade I: reflux into a nondilated ureter.
- Grade II: reflux into the upper collecting system without dilatation.
- Grade III: reflux into dilated ureter and/or blunting of calyceal fornices.
- Grade IV: reflux into a grossly dilated ureter.
- Grade V: massive reflux, with significant ureteral dilatation and tortuosity and loss of the papillary impression

The ureter is attached to the bladder in an oblique direction between the detrusor muscle and bladder mucosa. Reflux is prevented by the flap-valve mechanism created between them. VUR in children results in significant pyelonephritis. The inflammatory reaction caused by a pyelonephritic infection may lead to kidney injury or renal scarring. It is also known as reflux

nephropathy. VUR can occur as an isolated anomaly or it can occur secondary to other renal pathology. The pathogenic organisms ascend backwards and can result in renal scarring and injury.

The investigation of choice for detecting VUR is Voiding cystourethrography. The urinary catheter is placed and contrast is instilled into the urinary bladder by gravity dependent position. The contrast solution is kept at room temperature. When cold liquid is infused it will initiate an increased detrusor tone in young children and subsequently causes the bladder to empty at smaller volumes than warm liquids. Contrast medium should be instilled via the gravity drip method and never by hand injection. This prevents transmucosal contrast medium absorption and contrast reactions. Sudden push of contrast solution will cause a sudden rise of bladder pressure, which stimulates an unwanted premature bladder contraction at low volume. This could lead to underestimate any pathology and will result in inconclusive findings. Feeding tube is preferred for catheterisation instead of Foley catheter, since it has a smaller lumen relative to its outer diameter and is not suitable for VCUG. 5-F size feeding tube is appropriate for children under 1 year. Procedure should be explained to the parents as it create anxiety to them. Catheterization should be done by experienced personnel under strict aseptic precautions. The catheter should not be advanced any further than 1-2 cm after urine is collected. Now images are taken by serial radiographs by making the

child to void. After treating the active urinary infection and resolution of clinical symptoms , VCUG should be performed.

Indications for surgery :

- High grade reflux of type 4-5,
- When there is low chance of spontaneous resolution of symptoms,
- Scarring of the kidney,
- Recurrent urinary tract infections,
- Getting fever because of UTI, while on antibiotics continuous prophylaxis.
- Parental decision for surgery.

FDA approved the drug Deflux, a bulking agentfor the treatment of VUR from grades 1-4. 2010 guidelines of American urology association was revised for the patients having breakthrough febrile urinary tract infection to include endoscopy treatment.

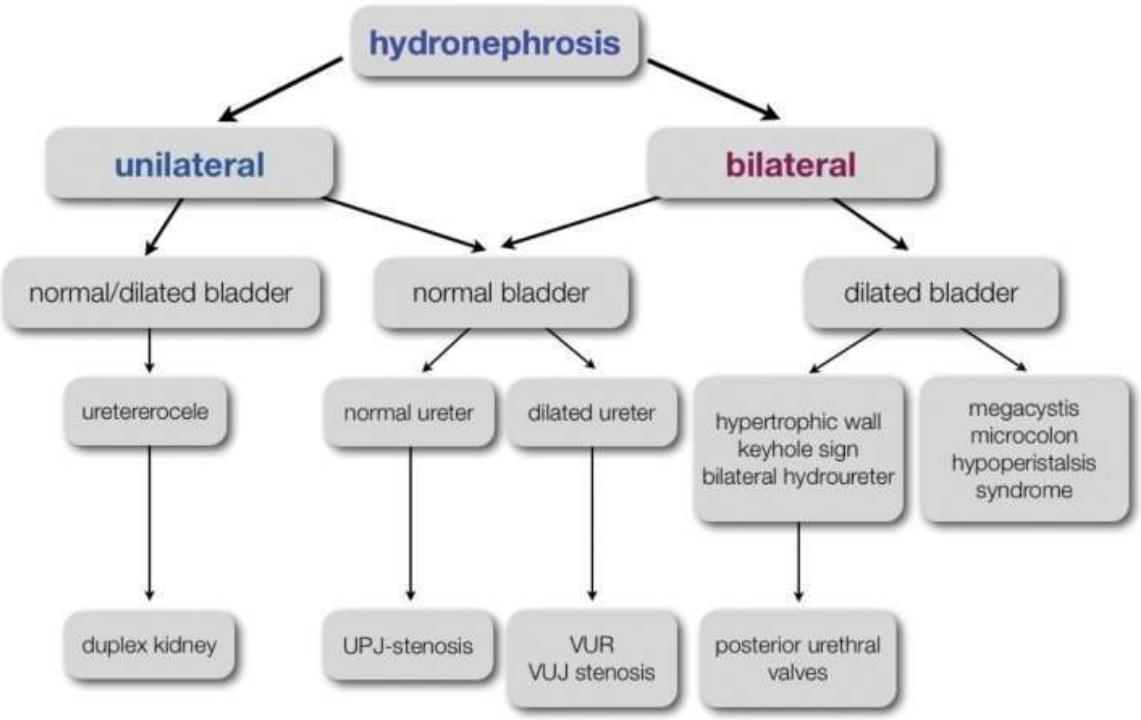
In a study by shaikh et al (26), mentioned that in systemic review of 33 studies for finding 99mtechnetiumdimercaptosuccinic acid (DMSA) scan abnormalities in children having urinary tract infection. They found that DMSA scan showing abnormalities in 57% of the children taken during acute

phase . Their features are consistent with findings of acute pyelonephritis.During follow up , scan 15% of the children had renal scarring.

Cooper et al mentioned in his study that the primary aim of surgical management is to prevent the febrile urinary tract infection and from pyelonephritis. But it is not yet proved that performing surgery will reduce the renal injury. Surgery will be benefitted in patients, having recurrent pyelonephritis and persistent reflux despite of conservative management. (27).

Evaluvation of antenatally detected CAKUT :

The hydronephrosis is the most commonly detected anomaly in the antenatal ultrasonography. The diverse etiology of fetalhydronephrosis is outlined as below.



Antenatal hydronephrosis is present whenthe foetal renal pelvis diameter is more than or equal to 4 mm during the 2nd trimester scan & more than or equal to 7 mm in 3rd trimester scan. It is classified into mild, moderate and severe based on renal pelvic APD size. The upper limit for a normal renal antero-posterior diameter in the third trimester is 7 mm. The AP diameter of more than or equal to 7 mm at 18 weeks (second trimester)denotes fetus with postnatal reflux or having obstruction. But those having same cut off at late gestation usually do not have significant pathology. There is always chance for inter observer variation and intra observer variation in measuring renal pelvic APD, since it is observer dependent. The renal pelvic AP diameter varies with gestational age, hydration status of mother and in bladder distension. (29).

In a study by Mallik M et al (34), concluded that the there is increasing sensitivity and accuracy of ultrasound screening at the time of 18–22 weeks. When APD of renal pelvis ≥4 mm , then the repeat scan at done after weeks of gestation. If the renal pelvis APD is ≥7 mm in the 2nd trimester then they should be referred to higher centre.

In study by sidhu et al (9), there is spontaneous resolution of antenatal hydronephrosis with renal pelvis APD less than 12 mm and SFU grade 1–2.

In study by lee at al (13), they found that the post natal renal anomaly is increased with the size of antenatal pelvic dilatation. Post natal renal anomaly persists in 11.9%patients with mild hydronephrosis, 45.1% of them with moderate hydronephrosisand 88.3% with severe hydronephrosis.

Classification of antenatal hydronephrosis based on renal pelvic anteroposterior diameter, APD (29)

Classification	Renal pelvic APD	
	Second trimester	Third trimester
Mild	4-6 mm	7-9 mm
Moderate	7-10 mm	10-15mm
Severe	>10mm	>15mm

In a study by Metzger et al (31), they concluded that severe hydronephrosis in postnatal scan has an positive correlation with the risk of urinary tract infection and surgery. There is negative correlation among those who had spontaneous resolutionofhydronephrosis in postnatal scan.

In study by Longpre et al (32), they reported that the risk of morbidity is low in those fetuseswho had minimal pelvic calyceal dilatation of 5-9mm. The morbidity is risk is more in the fetus having severe hydronephrosis with APD of more than 15mm, and these group need regular follow up.

In study by Sairam, Sasson et al ,88 % of them who were detected antenatally with mild hydronephrosis have resolution before birth or while

after birth during neonatal period. But 1/3rdof the neonates whom found to have moderate hydronephrosisand severe hydronephrosis during the 3rd trimester needed surgical intervention in the post natal period. Nearly eighty percent of the fetuses who were diagnosed in the 2nd trimester had resolution of the findings or improved. These babies had very low morbidity in the postnatal period. (33).

Sinha et al (29) proposed that, with antenatal detected unilateral or bilateral hydronephrosis does not warrant termination of pregnancy, expect the presence of extrarenal major structural anomalies.

Additional Parameters Evaluated On Antenatal Ultrasonography (29)

Renal Abnormalities :

- Oligohydramnios
- Dilated or thick-walled bladder
- Calyceal dilatation
- Ureteral dilatation
- Perinephric urinoma
- Keyhole sign

Loss of renal parenchyma, as suggested by:

(*i*) Cortical thinning,

(*ii*) Poor corticomedullary differentiation,

(*iii*) Increased renal echogenicity and /or

(*iv*) Renal cysts

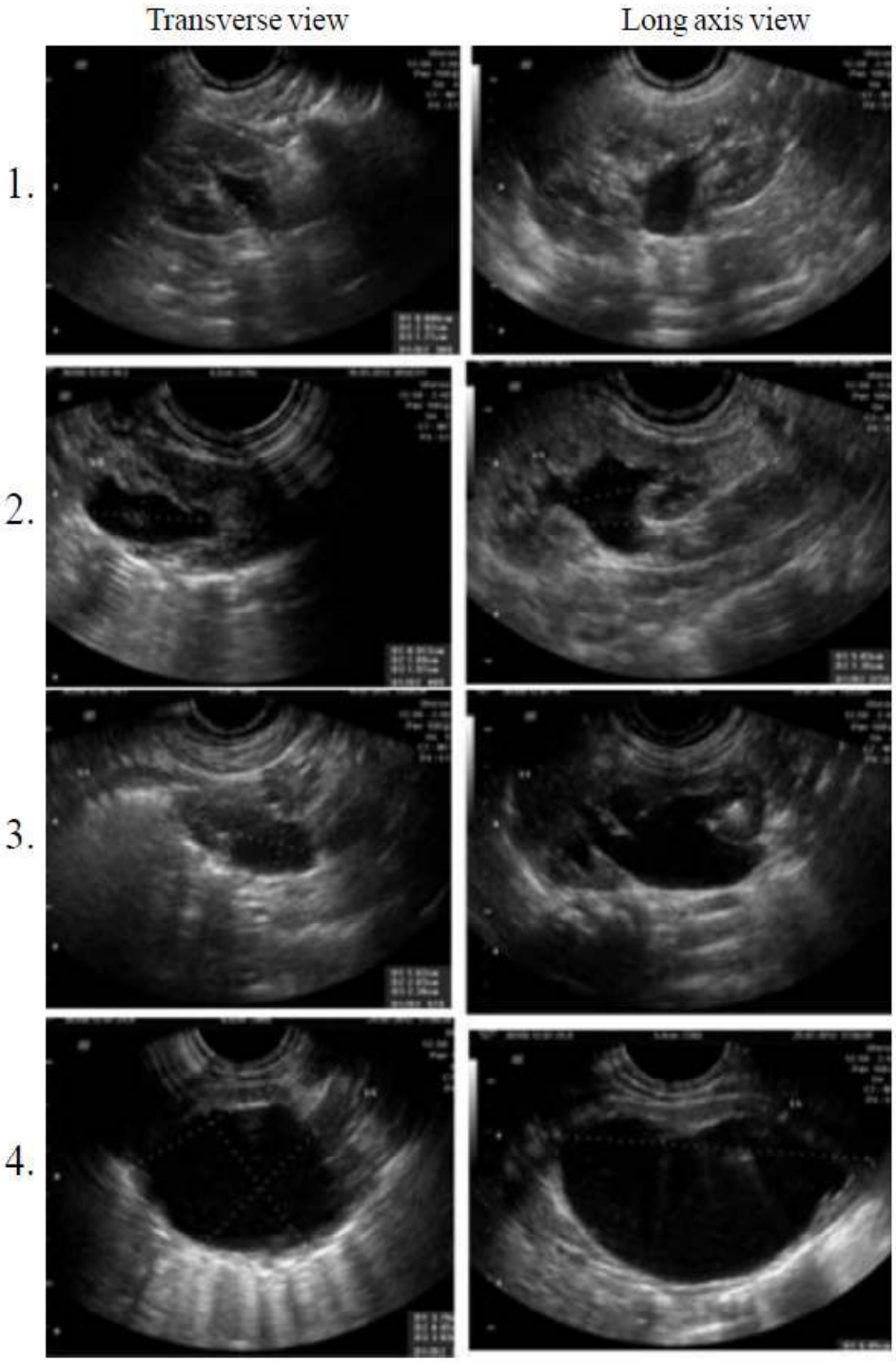
Soft signs:

• Increased nuchal translucency • Echogenic focus in the heart • Absent nasal bone • Shortened long bones (humerus, femur)	• Echogenic bowel • Choroid plexus cyst • Hydronephrosis • Ventriculomegaly

The common classifications for detection of postnatal hydronephrosis is based on SFU grading and based on size of renal pelvic antero-posterior diameter. SFU grading assess the renal pelvic fullness ,calyceal dilatation and the thickness of the cortex.(Lee et al, 13)

Postnatal USG depicting the different grades of hydronephrosis according to the Society of Fetal Urology (SFU) classification

- Grade 1: Slight separation the central renal echo complex.
- Grade 2: Renal pelvis is further dilated and a single or few calyces may be visualized.
- Grade 3: Renal pelvis is dilated and there are fluid filled calyces throughout the kidney, but renal parenchyma is of normal thickness.
- Grade 4: As grade 3, but renal parenchyma over the calyces is thinned.



Society fetal urology (SFU) grading

Infants detected to have unilateral mild hydronephrosis or with bilateral hydronephrosis, whose APD measuring less than 10 mm, or 1-2 grade by SFU classification can be followed only by ultrasound (29). Most of the cases resolve in first two years of life. Hence antibiotic prophylaxis is usually not necessary for mild hydronephrosis (Tombesi et al, 35).

Mallik et al, proposed that infants detected to have renal anteroposterior diametermore than 10 mm or grade 3-4 by SFU 3-4 at birth needs to be monitored closely during follow up period (34).

The other classification previously used for evaluvation of antenatal hydronephrosisare :

Anterior-posterior pelvic diameter (APPD) Grignon (1986), grading system (9)

Grade	Size of pelvis	Calyceal dilatation
Grade 1	1 cm	Physiological
Grade 2	1–1.5 cm	Normal calyces
Grade 3	>1.5 cm	Slight dilatation
Grade 4	>1.5 cm	Moderate dilatation
Grade 5	>1.5 cm	Severe dilatation and atrophic cortex

Blachar (1994), grading system (9)

Grade / Size of pelvis / Features

Grade 0<0.4 cm Normal/ no hydronephrosis

Grade 1 0.4–0.9 cm Detectable hydronephrosis

Grade 2 1–1.5 cm Significanthydronephrosis, rounding of calyces

Grade 3 >1.5 cm Severe hydronephrosis and calyces; cortical atrophy and distorted renal anatomy.

Sinha et al recommends VCUG is done for patients having unilateral hydronephrosis or bilateral hydronephrosis - pelvis AP diameter more than 10 mm, grade 3-4 by SFU grading or with ureter dilatation. Patients suspected to have lower urinary tract obstruction like PUV, VCUG should be performed early, between 24 to 72 hours of life. The procedure is done at 4 to 6 wks of postnatal life in others (29).

PUV in males (lower urinary tract obstruction) is an important cause for antenatal hydronephrosis, which requiresearly intervention and management. USG findings of PUV are thickened wall and dilated bladder that not emptying the urine, bilateral hydroureteronephrosis& urethra having dilation posteriorly. The risk for developing progressive kidney disease is increased in patients with PUV. Urinary tract infection risk is also high. VCUG should be done immediately after birth within 1-3 days of life.

Lee et al in a study, reported that 8-38% patients with antenatal hydronephrosis detected to have vesicoureteric reflex, whereas in general population< 1 % . The grade of VUR does not correlate with the severity of hydronephrosis. Some babies will be reported asnormal postnatal ultrasound despite of having VUR (7, 29). The patients with renal pelvis AP diameter more than 10 mm, likely to have severe vesicouretric reflux.

Diuretic Renography:

Diuretic renography is used for the evaluation of renal function and differentiation between the obstructive causes and non-obstructive causes of renal or ureteral dilation. It is a safe procedure and not very expensive. It estimates the relative renal function. The preferred radiopharmaceuticals are 99mTcmercaptoacetyltriglycine (MAG3), ethylenedicysteine (99mTc-EC) or Tc-diethylenetriaminepentaaceticacid. DTPA is relatively low cost and easily available. Radiotracer uptake is reduced inkidneys with reduced function.At 6-8 weeks of age ,renography is done. But in patients with severe HN and thinned cortex, the procedure can be done early. Hydration with iv fluids and catheterizing the bladder are not necessary. Oral hydration is adequate. Urinary catherizationshould be done in patients having poor bladder emptying, bilateral severe reflux or with megaureters.

The renogram curve is normal when there is an early peak within 2-5 minutes of drug administration, followed by a descending phase rapidly and finally almost complete elimination of the drug in 20 minutes.The elimination

of the drug depends on the hydration status and the composite and differential function of the kidney. Obstruction is ruled out if there is satisfactory elimination of the drug spontaneously, or after giving iv diuretics and after voiding.

When the curve is not declining even after 20 minutes remaining in ascending phase or in plateau phase, radionuclidedrug is not cleared even after giving diuretics and after voiding , then it is said to be obstructive renal curve (36). The differential function of kidneys between 45-55 % were considered normal. The kidney function is impaired, when the differential function is below 35% - 40% in the kidney with drainage obstruction. Obstruction should be considered when it takes long time to eliminate 50 % of the radionuclide drug and in ipsilateral kidney having supranormal function more than or equal to 55 %.

Sinha et al recommends radionuclide imaging for the infants who have moderatehydronephrosis to severe hydronephrosisand not havingvesicoureteric reflux (29).

Guidelines for standard and diuretic renogram in children : (36)

Pre-requisites:

- Ensure adequate hydration.
- Oral hydration is sufficient.
- Administer an additional feed prior to study, if necessary.

Bladder catheterization

- Catheterization is not necessary in all patients.
- Usually done in patients with suspected bladder abnormality or post micturition films showing persistent contrast in the bladder.

Radiopharmaceutical agent used :

- 99mTc-MAG3 (99mTechnetium mercaptoacetyltriglycine)
- 99mTc-DTPA (99m Technetium diethylenetriaminepentaacetic acid)
- 99mTc-EC (99m Technetium ethylenedicysteine)

Dose:

- 99mTc-MAG3: 1.9 MBq per kg body weight (minimum 15 MBq)
- 99mTc-DTPA: 3.7 MBq per kg body weight (minimum 20 MBq)
- 99mTc-EC: 50–100 MBq
- The dose is reduced in impaired renal function.

Diuretics:

- Frusemide 1 mg/kg IV
- Timing: Simultaneously with radiopharmaceutical (F0); alternatively given 20 minutes following (F+20) or 15 minutes prior (F-15)

Position :

- Patient kept in supine position for first 20 minutes.
- Erect position is kept if drug clearance is delayed.

Acquisition:

- Differential renal function assessed at 1-2 minutes after administration of radiopharmaceutical drug.
- Renogram curve is inspected at 20 minutes
- Post micturition films taken 50-60 minutes after tracer injection.

Interpretation:

- A curve that shows an early peak (2-5 minutes) followed by complete emptying, either spontaneously, after frusemide, or on late post micturition film, excludes obstruction.
- An obstructive pattern is a curve that rises continuously over 20 minutes or appears as a plateau, in spite giving frusemide and post micturition.

Indications for surgery in CAKUT :

Surgery is indicated for patients with obstructed hydronephrosis(lower urinary tract obstruction) , those with reduced differential kidney function and those who worsen during the follow up evaluvation. Pyeloplasty is considered by most experts for patients who have obstructed HN, those with renal differential function < 35 %, and abnormalrenogram with prolonged elimination time of radionuclide drug (t ½ more than 20 minutes) (29) . When

the renal function is worsening progressively correlating with reduction in reduced by renal differential function by > 5-10 % , then pyeloplasty is recommended. (46).

Antibiotic prophylaxis:

The antibiotic prophylaxis is recommended for the babies who have severe hydronephrosis, hydroureteronephrosis and those who detected to have Vesicouretric reflux. Antibiotics should be given for 1 year in those found to have severe VUR. The recommended antibiotics is cephalexin (dose is 10 mg/kg/day) for first three months of life. For more than 3 months the recommended antibiotics are cotrimoxazole (dose 1-2 mg/ kg/day) and nitrofurantoin(dose is 1 mg/kg/day) (29).

Antibiotic prophylaxis is recommended by American Urological Association (AUA)for the babies having severe VUR, for grades III-V (48).

In study by Kim et al, they reported that 19 – 36.2 % patients developed urinary tract infection , who were diagnosed to have moderate hydronephrosis or severe hydronephrosis due to obstruction(49). In study by Coelho et al , concluded that risk of infections is very high in babies with renal pelvic AP diameter of >10 mm in the postnatal scan.

Urinary tract infections (UTI): Pyelonephritis was defined as fever >38.0 °C, elevated C-reactive protein (CRP), leucocyturia and bacteriuria (≥105 CFU/ml; urine collected by catheter). Cystitis was defined as UTI with

neither fever nor elevated CRP.(43) The most common organisms causing are E.Coli , Klebsiella species, Proteus etc.

Urine culture is indicated in neonates with urogenital anomalies and in neonatal sepsis to exclude urinary tract infection.5ml of urine sample is obtained in a sterile container by supra pubic puncture,bladder catheterization or clean catch of midstream urine.Urine analysis is done for leucocyte esterase , nitrites and microscopy and findings are correlated with urine culture reports.

UTI may be diagnosed in the presence of one of the following:

(a) >10 WBC/mm3 in a 10 mL centrifuged sample

(b) >104 organisms/mL in urine obtained by catheterization and

(c) any organism in urine obtained by suprapubic aspiration.

Postnatal evaluation of patients with antenatal hydronephrosis in nut shell (29):

- Ultrasound scan is postnatal period is donebetween 3 to 7 days of life. Situations like suspected lower urinary tract obstruction scan is done earlier.

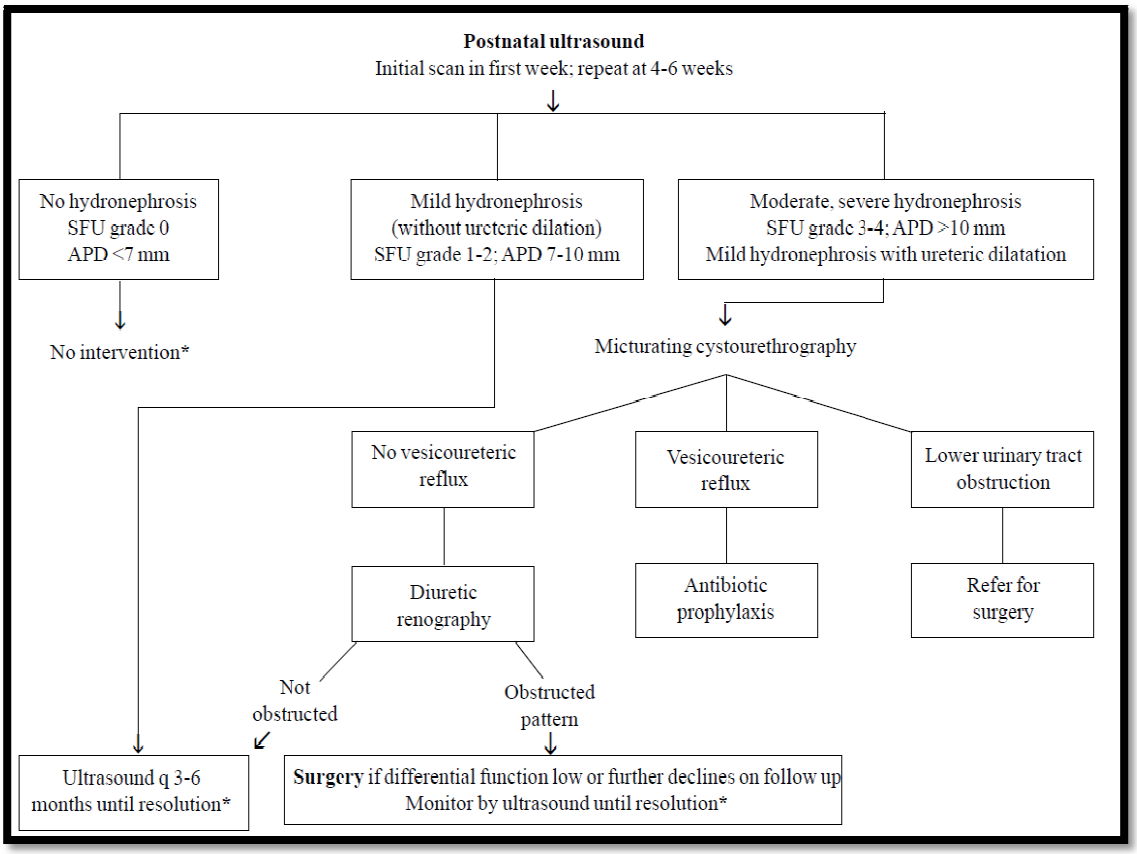
- Hydronephrosisin postnatal scan was classified based on SFU grading or renal pelvisAPD classification.

- Patients having mild unilateral hydronephrosis / bilateralhydronephrosis to be followed up in postnatal period with serial ultrasound scans, at 3 months and 6 months, and then till 12 months followed up monthly till

resolution. Close monitoring and evaluvation is needed for the ones with worsening hydronephrosis.

- Severe grades of hydronephrosis and hydroureteronephrosis should be evaluate for underlying cause such as obstruction or VUR.
- Diuretic renography detects the obstructive conditions and is useful in deciding on surgery.
- The risk of getting urinary tract infections should be counselled to parents of infants with hydronephrosis.

Postnatal Mx Of (ANH)Antenatally detected hydronephrosis (29) :



AIMS & OBJECTIVES

Primary objective :

To study the prevalence and pattern of distribution of antenatally diagnosedCongenital anomalies of kidney and urinary tract (CAKUT)in live newborns during a one year period.

Secondary objective:

To study the morbidity and postnatal outcome of antenatally detected CAKUT.

METHODOLOGY:

Study design: Prospective observational study

Study period:1st May 2015 to 30thApril 2016 (1 year)

Study locale: PSG Hospitals , Coimbatore.

All women attending the antenatal clinic of the Obstetrics & Gynaecology department have an antenatal ultrasound during the second trimester (between 20-24 weeks) and third trimester above 30 weeks of gestation. All those who were detected to have CAKUT either during the second or third trimester Ultrasound scan were included in the study, provided they delivered in this hospital. The ultrasound machine used Voluson E8 version 10.0.3 and ultrasound scan was done by the consultant obstetrician trained in sonology, during the antenatal period. All antenatal data were recorded. The antenatal anomalies were classified based on the Society for fetal urology grading and renal pelvis APD classification (29). Written informed consent was obtained from the parents after the baby was born. Both term and pre term babies were included in the study.

The first post natal scan was donebefore 7 days of life, the second between 4-6 weeks and the third between 4 – 6 months of age. Post natal ultrasound scan was done by machine Philips IU 22 with matrix, and done by the consultant radiologist. Postnatal CAKUT classification was done as per SFU grading (29). To minimize the inter observer variation all the post natal

USG images were analysed by single person expertized in USG. All patients were followed up in consultation with the pediatric surgeon. Urine cultures, investigations and management were done at the discretion of the attending surgeon.

RESULTS

During the study period there were 2614 live births in the hospital, who fulfilled the inclusion criteria. Among them, 111 babies were eligible for the study. 3 parents refused consent. 108 babies (79 males and 29 females) were included in the study. Among them, 54 were found to have renal anomalies in the 2nd trimester scan. 20 of these normalised in the 3rd trimester scan, however an additional 54 with anomalies were detected.

In the second trimester scan anomalies were detected in 54 cases. Unilateral hydronephrosis in 28 , bilateral hydronephrosis in 23 , hydroureteronephrosis in 2 and 1 unilateral multicystic dysplastic kidney . Among the 28 with unilateral hydronephrosis, 14 normalised , 9 persisted , 4 became bilateral hydronephrosis and 1 was reported as multicystic dysplastic kidney during the third trimester scan . In 23 bilateral hydronephrosis , 6 normalised , 5 became unilateral hydronephrosis , 11 remained same and 1 was reported as posterior urethral valve during the third trimester scan.

Of the 20 who had an anomaly in the second trimester, but was normal in the third trimester, 14 were unilateral hydronephrosis, while the remaining were bilateral hydronephrosis. On follow up with postnatal scans, 18 of them continued to be normal, while 1 each with unilateral and bilateral hydronephrosis were reported abnormal in the first post natal scan. However, both of them became normal by the second post natal scan.

In the 3rd trimester scan, 88 babies were noted to have anomalies. Of them, 51 babies had unilateral hydronephrosis , 29 had bilateral hydronephrosis , 5 had multicystic dysplastic kidneys and 3 had posterior uretheral valve with bilateral hydroureteronephrosis.

All 108 babies had post natal Ultrasound done. In the 1stPost natal scan 65 babies were reported to have normal USG. Among these 65 babies, 34 had unilateral hydronephrosis, and 13 bilateral hydronephrosis in the third trimester scan, while the remaining 18 were those reported abnormal in the second trimester scan, but was normal in the third trimester scam.

43 babies had persisting anomalies in the 1st post natal scan. Among them, 20 had unilateral hydronephrosis (the 3rd trimester scan of these 20 patients showed 11 with unilateral hydronephrosis,7 with bilateral hydronephrosis, 1 with PUV and bilateral hydroureteronephrosis and 1 was normal), 11 bilateral hydronephrosis (the 3rdtrimester scan of these 11 patients showed 4 with unilateral hydronephrosis and 7 with bilateral hydronephrosis) ; 3 unilateral hydroureteronephrosis (the 3rd trimester scan of these 3 were 1 unilateral hydronephrosis , 1 bilateral hydronephrosis and 1 normal); 3 bilateral hydroureteronephrosis (their 3rd trimester scans were 1 bilateral hydronephrosis and 2 bilateral hydroureteronephrosis) ; 4 multicystic dysplastic kidney (their 3rd trimester scan had same findings of multicystic dysplastic kidney) , 1 had unilateral bulky kidney with normal parenchyma and no calyceal dilatation (the 3rd trimester scan was unilateral hydronephrosis)

and 1 was medullary nephrocalcinosis with bilateral hydroureteronephrosis (3rd trimester scan was bilateral multicystic dysplastic kidney).

Among the 43 babies who had abnormal findings in the first scan, 12 cases normalized in the second post natal scan.. 9 unilateral hydronephrosis , 1 bilateral hydronephrosis , 1 unilateral and 1 bilateral hydroureteronephrosis .

Among the 31 with abnormal second scans, 4 were lost to follow up. Of the remaining 27, nine were reported normal in the 3rd post natal scan. 5 with unilateral hydronephrosis , 3 bilateral hydronephrosis and 1 unilateral hydroureteronephrosis.

In the remaining 18 cases, 6 had undergone surgery , 4 persisted as Multicystic dysplastic kidney , 1 had medullary nephrocalcinosis, 1 unilateral bulky kidney, 4 had unilateral hydronephrosis and 2 had bilateral hydronephrosis. They are on follow up.

Overall, among the 108 babies detected to have CAKUT on antenatal Ultrasound, 86 (79%) normalized without any intervention by 4-6 months of age, 6 required surgical intervention, 4 were lost to follow up and the remaining 12 babies (4 multicystic dysplastic kidneys, 1 medullary nephrocalcinosis, 4 unilateral hydronephrosis 2 bilateral hydronephrosis and 1 unexplained bulky kidneys) were under follow up.

Clinical course of babies who had surgery and their outcome:

Baby 1 presented at 1 month of life with symptoms of UTI. Antenatally diagnosed as Posterior uretheral valve with bilateral HUN was on chemoprophylaxis . Urine culture has grown Escherichia Coli. Sr. creatinine was 0.48 mg/dl. DMSA was done. Cystoscopy and fulgration procedure was done. Discharged on antibiotic prophylaxis. On follow up baby was thriving well .

Usg showing bladder and dilated ureter

USG showing Ureterohydronephrosis

MCU showing bilateral VUR

DMSA showed mild reduced cortical function of left kidney and small possible scar in upper pole.

Differential function :

Left kidney : 45% ;

Right Kidney : 55 %

Baby 2 with antenatal diagnosis of right PUJO was admitted at 1 ½ months of age following 2nd post natal scan . It was found to have increase in renal pelvis diameter. Right renal pelvis APD was 30 mm with parenchymal thinning. DTPA showed decreased renal function. Dismembered pyeloplasty was done . Post op baby was doing well. At 6 months follow up renal pelvis APD was 8mm .baby doing well , no features of UTI and renal parameters are normal.

Pre op USG showing pelvic calyceal dilatation

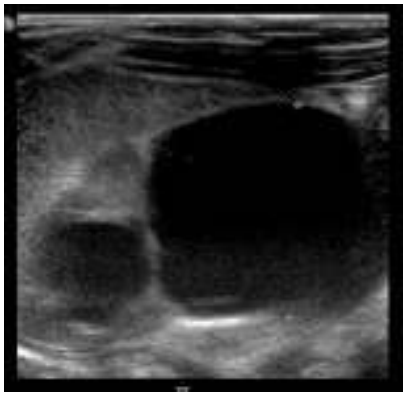
USG – Thinned out parenchyma

DTPA : LK – 74% ; RK – 26 %
Hydronephrotic obstructed right kidney with reduction in cortical function

After 3 months

After 6 months

Baby 3 with antenatal diagnosis of bilateral hydronephrosis – Right PUJO and left minimal dilatation was admitted at 3 months of age for surgery. APD was increasing with calyceal dilatation 29 mm .DTPA report was 45 % with obstructive pattern. Dismembered pyeloplasty was done. Baby was doing well at follow up.



Pre- Op: Balloned out pelvis

MCUG – No reflux

DTPA : LK - 55% ; RK – 45% function.

Post op : after 9 months

Baby 4 with antenatally diagnosed b/l HUN with PUV. Fulgration was done on day 2 of life. At 5 months of age Child admitted with for UTI . child was treated with antibiotics . After 2 weeks child presented with recurrent UTI . Child was operated – Cystoscopy + refulgration+ circumcision done. DMSA done .lk -48% ; rk – 52% no evidence of scarring.In further follow up, at 6 months weight was 6.22 kg and renal parameters was normal.

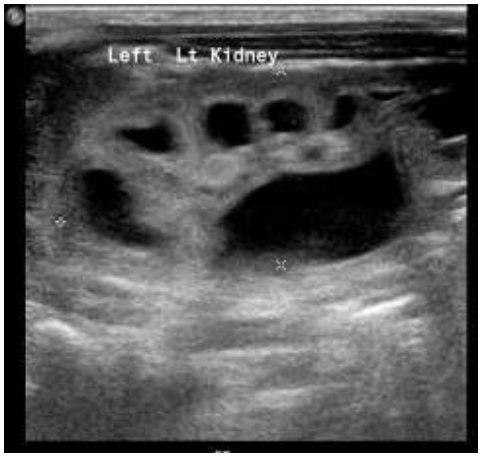
USG showing bilateral UHN with thickened bladder – pre op

DMSA: L.K - 48% (no evidence of scarring)

R.K – 52% (no evidence of scarring)

Post operative ultrasound – after 6 months – bilateral minimal hydronephrosis

Baby 5 with antenatal diagnosis of b/lhydronephrosis – leageft side severe hydronephrosis PUJO and thinning of parenchyma . child was on chemoprophylaxis. At 5 weeks follow up scan showed Left PUJO. At 2 ½ months DTPA showed 29 %. Renal pelvis APD was 25 mm . Dismembered pyeloplasty was done.



Pre-op USG

DTPA : Hydronephrotic , obstructed left kidney with evidence in cortical function

Normal functioning , non obstructed right kidney

LK – 29 % ; RK- 71 %

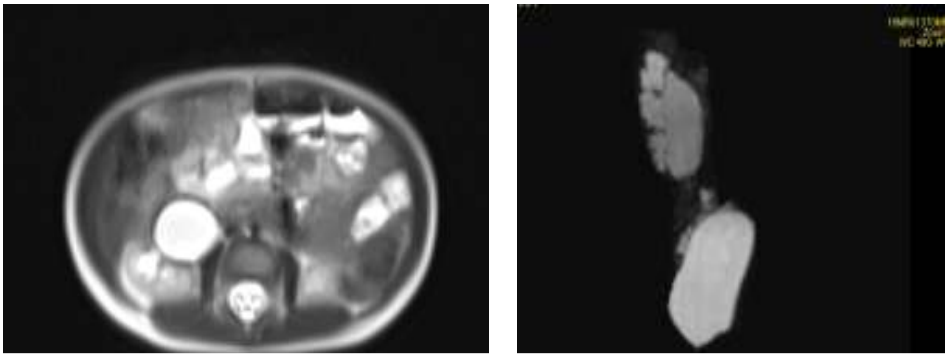
Post op USG

Baby 6 with antenatal diagnosis of u/l Hydronephrosis with PCD – 1.74cm. Post natally was on follow up. PN1 scan showed APD of 15 mm .child was given chemoprophylaxis. At 5 months the finding was u/l HUN .on further follow up at 9 months of age child had DTPA – RK 46 % ; LK 54% with decreased perfusion and cortical function – suggestive of partial PUJO. APD was 32mm at time of surgery. Pyeloplasty was done.

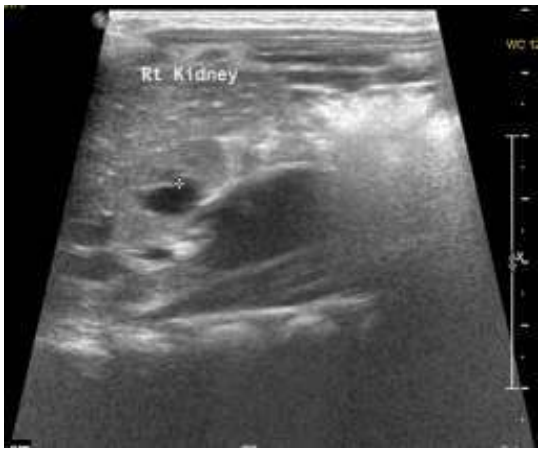
Pre-op USG

DTPA – RK 46 % ; LK 54% with decreased perfusion and cortical function – suggestive of partial PUJO

b/o 6 continued…..



MRI images – Suggestive of right PUJO



Post op USG – right mild hydronephrosis

1 baby with nephrocalcinosis in our study was a nicu graduate. Preterm, 33week + 1 day, birth weight of 1.05 kg. Renal parameters were assessed at birth and 5 months of age were normal . Sr. creatinine was 0.38 .Baby was on regular follow up. Thriving well.

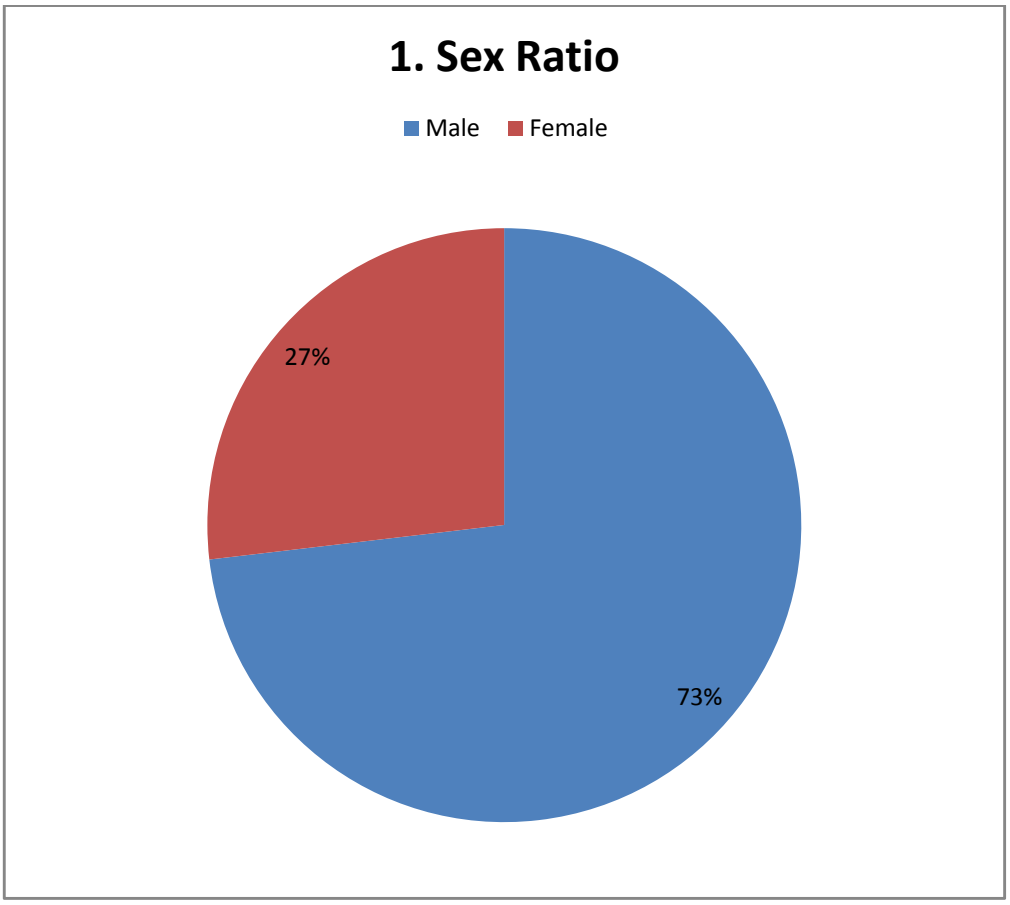
USG of a baby with Medullary Nephrocalcinosis

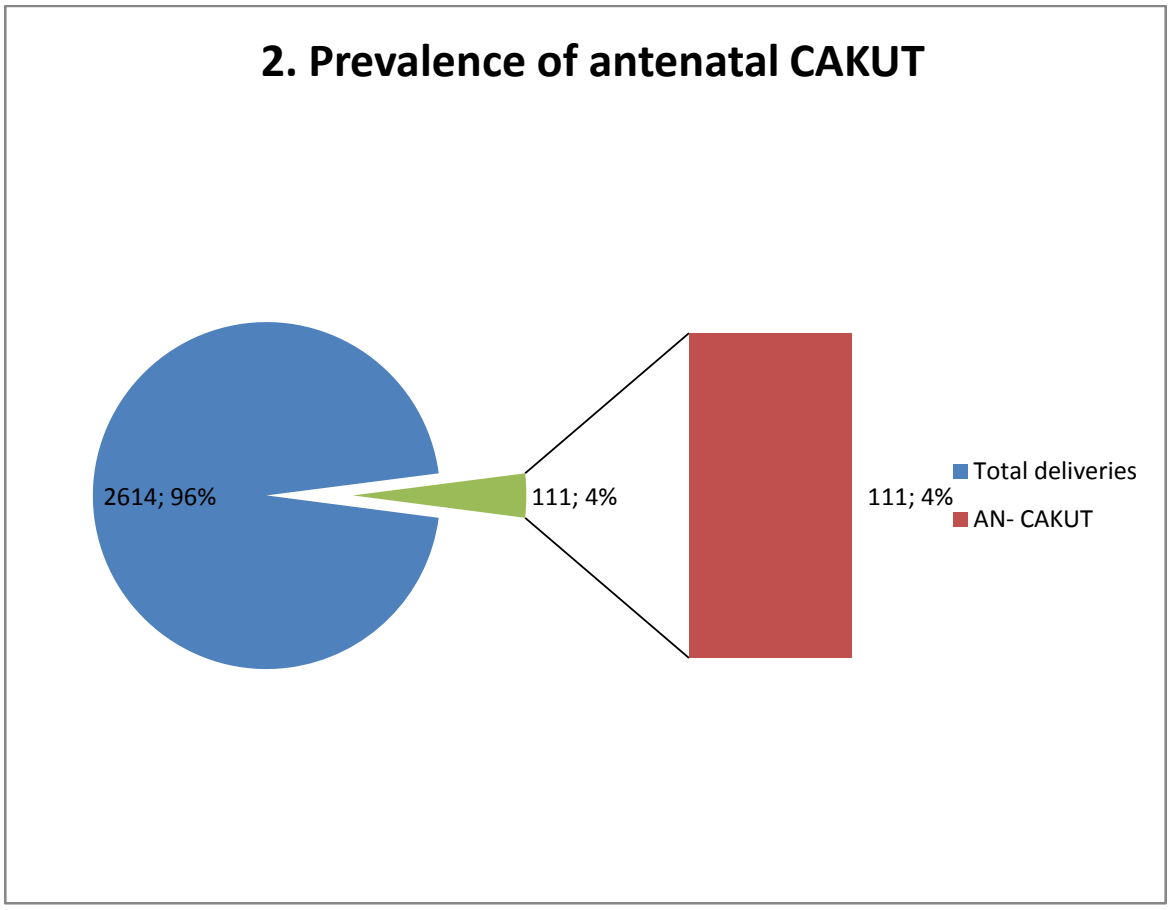
Table 1 :

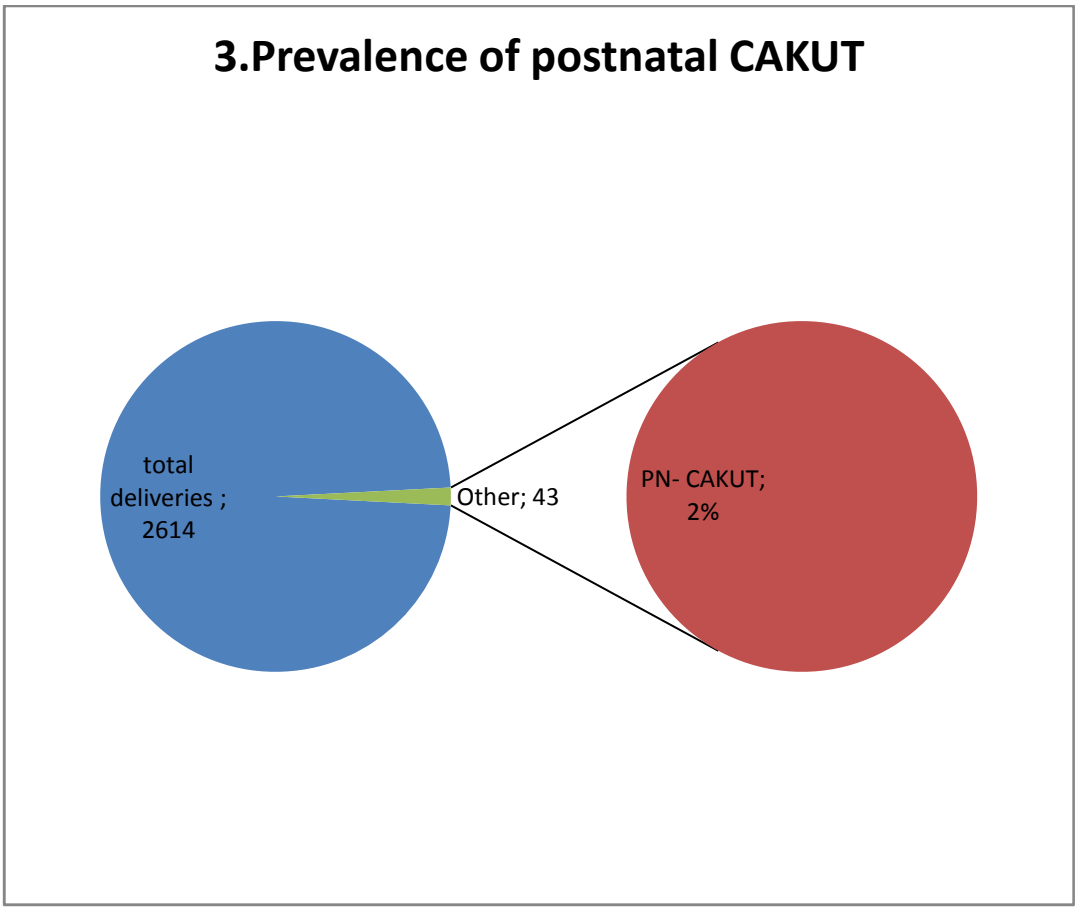
Sex distribution

Sex	Frequency	Percent
Male	79	73.1
Female	29	26.9
Total	**108**	**100**

Diagrams




2. Prevalence of antenatal CAKUT
2614; 96%
111; 4%
111; 4%
Total deliveries
AN- CAKUT


3.Prevalence of postnatal CAKUT
total deliveries ; 2614
Other; 43
PN- CAKUT; 2%

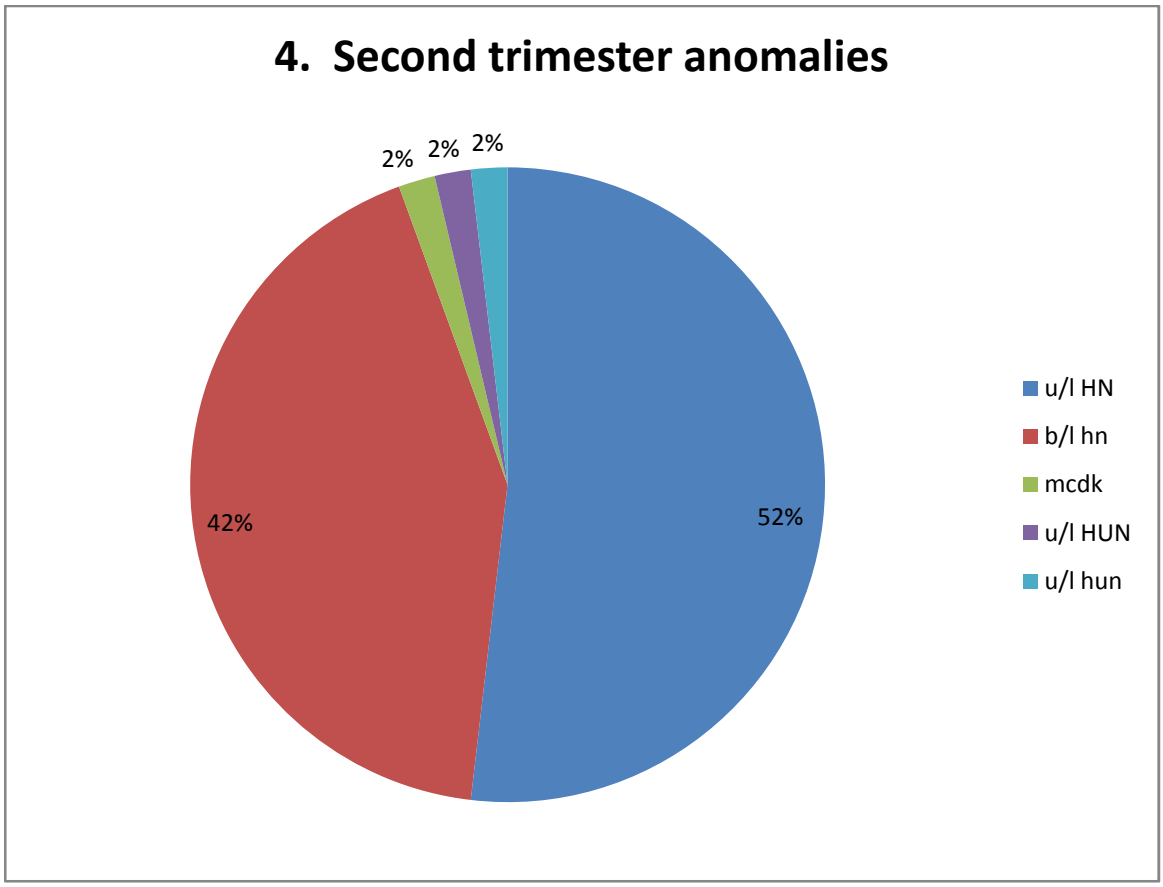

4. Second trimester anomalies
2%
2%
2%
42%
52%
u/l HN
b/l hn
mcdk
u/l HUN
u/l hun

Table 2 :

Prevelance of 2nd trimester anomalies

2nd trimester anomalies	**Frequency**
unilateral HN	28
bilateral HN	23
unilateral HUN	1
bilateral HUN	1
unilateral MCDK	1
Total	**54**

Table 3 :

2nd trimester anomalies and their fate in 3rd trimester

2nd trimester scan anomalies	Total No	Fate of these anomalies in 3rd trimester scan						
		Normal	U/l HN	B/l HN	U/l HUN	B / l HUN	MCDK	PUV
U/l HN	28	14	9	4	-	-	1	-
B/l HN	23	6	5	11	-	-	-	1
U/l HUN	1	-	-	-	-	-	1	-
B/l HUN	1	-	-	-	-	-	-	1
MCDK	1	-	-	-	-	-	1	-
Total	54	20	14	15	-	-	3	2

Table 4 :

Anomalies in 3rd trimester

3rd trimester scan	Frequency	Percent
Normal	20	18.5
unilateral HN	51	47.2
bilateral HN	29	26.9
unilateral MCDK	4	3.7
bilateral MCDK	1	0.9
B/L hun+puv	3	2.8
Total	**108**	**100.0**

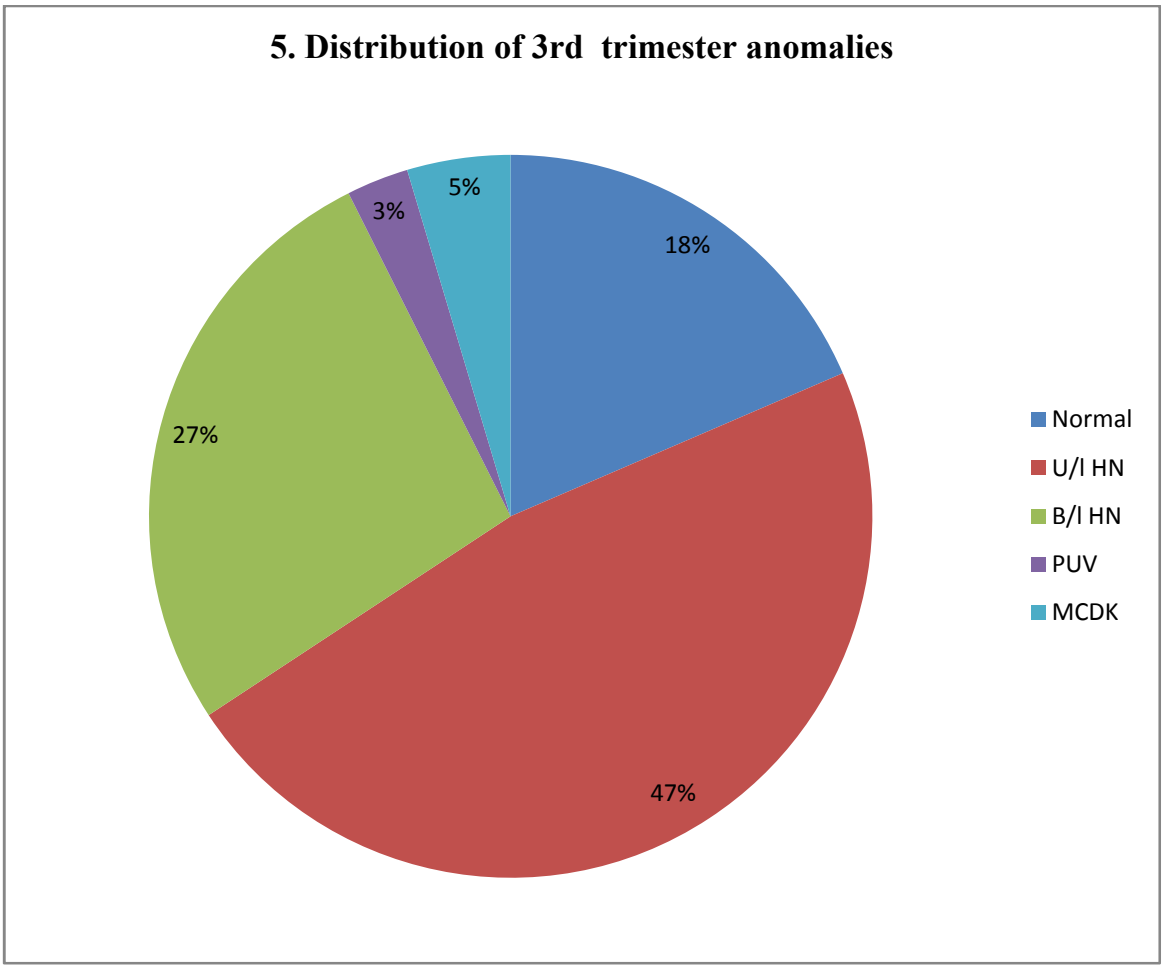

5. Distribution of 3rd trimester anomalies
18%
47%
27%
3%
5%
Normal
U/l HN
B/l HN
PUV
MCDK

Table 5 :

3rd trimester anomalies and their fate in 1st P.N scan

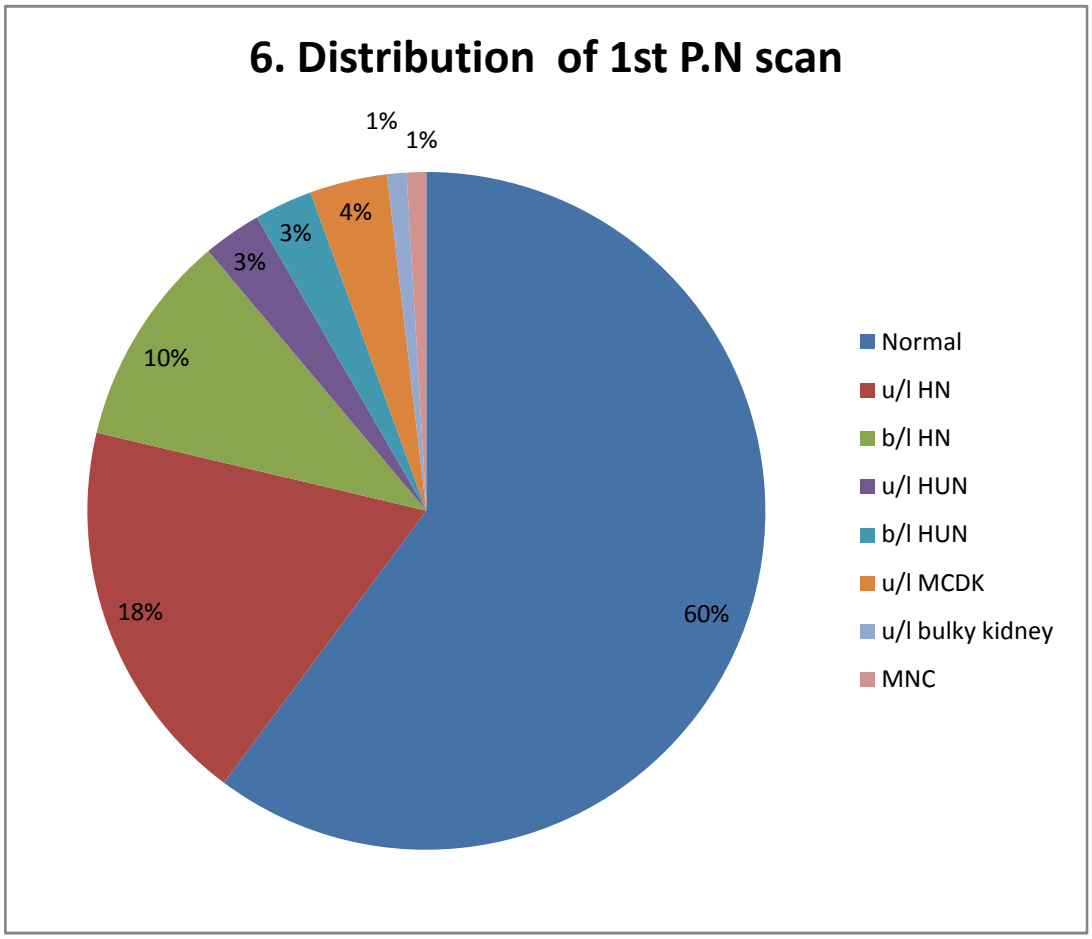
3rd trimester scan anomalies	Total No	Fate of these anomalies in the 1st post natal scan						
		Normal	U/l HN	B/l HN	U/l HUN	B / l HUN	MCDK	PUV
Normal	20	18	1	-	1	-	-	-
U/l HN	51	34	11	4	1	-	-	1
B/l HN	29	13	7	7	1	1	-	-
U/l HUN	-	-	-	-	-	-	-	-
B/l HUN	-	-	-	-	-	-	-	-
u/l MCDK	4	-	-	-	-	-	4	-
b/l MCDK	1	-	-	-	-	-	-	1
PUV	3		1	-	-	2	-	-
Total	108	65	20	11	3	3	4	2

Others : 1 u/l HN in 3rd trimester scan is reported as bulky kidney ; b/l MCDK is reported as medullary nephrocalcinosis.

Table 6 :

Distribution of 1st postnatal scan anomalies

1st post natal scan anomalies	Frequency	Percent
Normal	65	60.2
u/l HN	20	18.5
b/l HN	11	10.2
u/l HUN	3	2.8
b/l HUN	3	2.8
ul MCDK	4	3.7
Medullary Nephrocalcinosis	1	0.9
unilateral bulky kidney	1	0.9
Total	**108**	**100.0**



Distribution of 1st postnatal USG – renal anamolies

Table 7 :

Anomalies persisted during 2nd postnatal scan

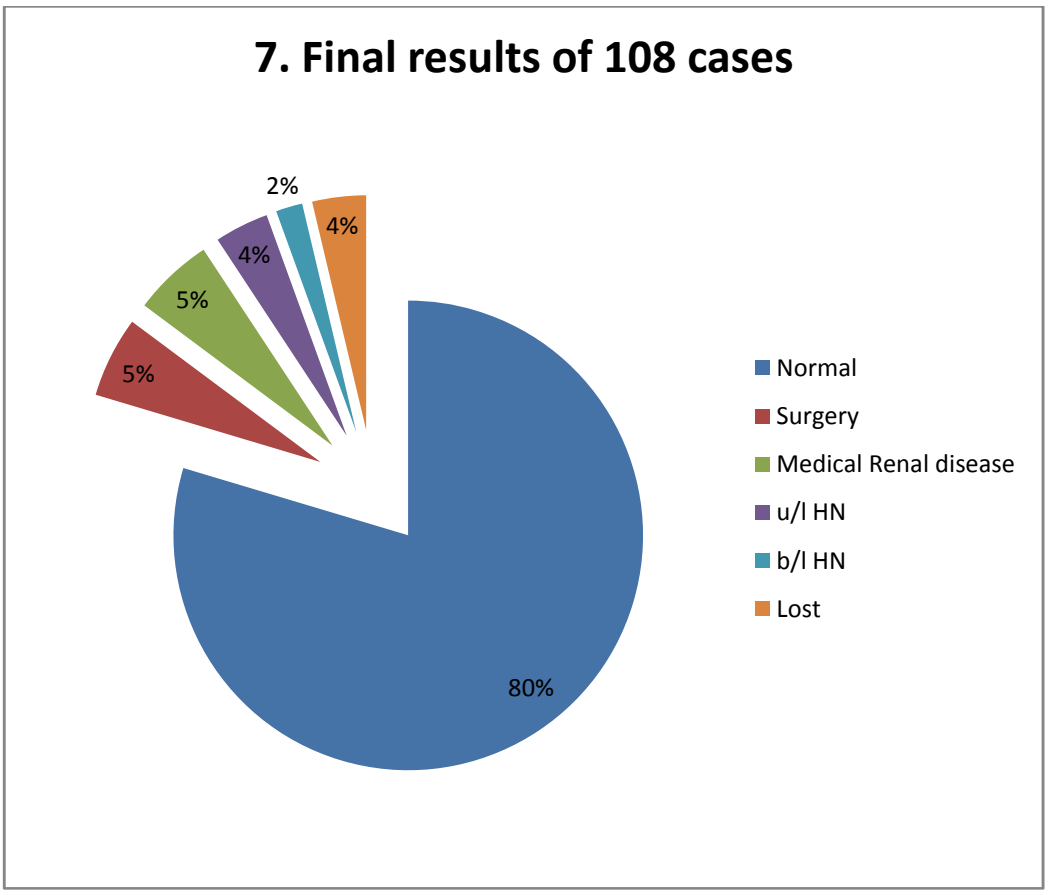
Follow up cases in PN scan 2	**Frequency**
Lost to follow up	4
Normal	12
MNC+b/l HN	1
u/l HN	12
b/l HN	6
u/l HUN	1
b/l HUN	2
U/l MCDK	4
u/l bulky kidney	1

Table 8 :

Fate of babies with CAKUT during 3rd post natal scan

Fate of Babies With CAKUT At III PN Scan	Frequency
Normal in PN scan 3	9
Unilateral HN	4
Bilateral HN	2
Unilateral MCDK	4
Medullary nephrocalcinosis	1
Bulky kidney	1
Surgery	6
Lost to follow up	4
Total	**31**

Final analysis of 108 samples



Medical renal disease – 4 MCDK, 1 Medullarynephrocalcinosis, 1 Bulky kidney.

DISCUSSION

Antenatally detected urinary tract abnormalities are the commonest anomalies detected on prenatal ultrasonography accounting for 20–50 % of all congenital disorders (5).The prevalence of the CAKUT in our study is 42.4 / 1000 live births. The study conducted in a tertiary care centre, in Saudi Arabia by Sallout B et al, reported thatantenatal prevalence of CAKUT is 21.28 per 1000 pregnancies and a birth prevalence of 19.80 per 1000 live births(1). To the best of our knowledge, there is no comparable study published from India.Study by jothi et al incidence of fetal urinary tract anamolies was 0.75%(44).

Antenatally diagnosed hydronephrosisprevalence ranges from 0.6 % to5.4% by Sinha et al(29). In a study done by bondagji, the antenatally detected CAKUT prevalence is 3.26 per1000 births (41).In developed countries, the CAKUT prevalence in live and stillborn infants is 0.3 to 1.6 per 1000(41). In a large study conducted in Europe, multicentre study, the details was taken from 20 registries of 12 countries. The study was done to evaluvate the prevalence of renal anomalies in antenatal ultrasound scan included all live born and stillborn (datas collected from 709030 births- both live and still birth). They found the mean prevalence to be 1.6 per 1000 live births. (41)

Epidemiological prevalence of CAKUT in the developing world is lacking. The studies on prevalence of CAKUT in India were limited.More so

over there are no studies in high risk population to estimate their prevalence, clinical course and outcome in the developing world (3).

There was a significant male preponderance in our study with 79 males and 29 females, giving a ratio of 2.7:1. In study done by Gokce et al (5), the antenatal renal abnormalitiesappeared to be primarily a problem of boys (187 males, 69 females; with a M:F ratio of 2.71: 1). In a study done in Iran done by SadhegjiBojd et al , they screened 200 patients of post natal hydronephrosis, the male to female ratio is 3.5:1 (40). In brazil study done by Isabel Quirino et al , have male predominance . The study was done on 822 children with CAKUT of which 557 are male and 255 are female (28). In study done by Abishek et al, done in Telegana, India the distribution of their study subjects according to the sex of the baby were 76.1% were male compared to only 23.9% of females.(30)Other studies have also reported a male preponderance.(3, 41, 44).

In the study done by gokce et al (5) the antenatal ultrasound findings is changed in almost one-sixth (16 %) of the cases at postnatal US examination. Another study reported by Najmaldin et al, (37) errors included inability to distinguish between mostly cystic dysplasia and hydronephrosis and between hydronephrosis and normal patients.

In this study to reduce the discrepancies in coining the terminologies the postnatal images of the study population was reviewed by the expert team individually and analysed. In our study involvement of right kidney and left

kidney were termed as unilateral involvement, if both were involved it was termed as bilateral involvement. The abnormalities found in the study are hydronephrosis, multicystic dysplastic kidney (MCDK), medullary nephrocalcinosis, posterior uretheral valve and an abnormal variant with large unilateral kidney. In the antenatal scan the kidney size , parenchyma texture , ureter , bladder , amniotic fluid index was noted. In the post natal scans kidney echotexture , enhanced renal echogenicity , pelvic calyceal dilatation , renal pelvis APD, ureteric dilatation and bladder wall abnormalities were documented. Associated anomalies if any were documented. The most frequently detected anomaly on antenatal ultrasound is hydronephrosis .Most of the affected patients have no other renal problems. This was termed as isolated antenatal hydronephrosis. (9).

In our study majority of the detected cases were hydronephrosis. In second trimester scan 54 out of 108, nearly 50% of the study population had renal anomalies . The majority was hydronephrosis.

In our study hydronephrosis is the commonest anomaly picked up in third trimester scan, 91 % of which 58% were unilateral hydronephrosis and 33% were bilateral hydronephrosis. Hydronephrosis was diagnosed in 51.1% of the cases (34). In a study by Saini et al ,hydronephrosis was the most common anomaly identified on postnatal scan (71%) that correlated well with the antenatal records (78%) (3).

In study by jyoti et al hydronephrosis was the most commonly detected anomaly 79% out of 100 cases. On evaluation of babies with moderate to severe hydronephrosis persisting abnormality was seen in 17.4% and 1.1%. 8 babies had surgical intervention of which 20 babies with severe abnormalities. Mild hydronephrosis was resolved in 75% of the cases.

20 cases out of 54 (37 %) had a normal scan at third trimester, but had abnormal record in second trimester were followed up postnatally. Saini et al , reported that all babies detected to havehydronephrosis detected in antenatal scan, for whom it had resolved prenatally should also be evaluated in the postnatal period (3). Lee et al , in his meta-analysis study, (13) reported that in every dilatation of the urinary tract, 36 % of them had high risk for developing uropathy , irrespective of the dilatation . Thus, prenatal diagnosis of any form of hydronephrosis warrants for a critical followuppostnatally for prevention of urinary infections and further renal damage.(29).

All the 108 babies in our study had post natal scan were done before the discharge from hospital. The mean day of USG was on day 3-5 of life. In the normal neonate, there is low urine output during the first 24–48 hours so that with unilateral hydronephrosis the USG should not be undertaken before 72 hours post-delivery. The severity of hydronephrosis was graded as per APD diameter and Society of fetal urology grading.

In our study 1st postnatal scan out of the 108 cases, 65 were normalised (60%). In studyby sidhu et al, their results demonstrate that more than 70% cases of mild hydronephrosis (SFU grades 1–2; APPD less than 12 mm) resolved, stabilized or improve during follow-up. Ismaili et al concluded in his study that babies whose hydronephrosis had resolved spontaneously in postnatal period do not require further follow up and they have good outcome (38). In a cohort study of 130 infants with antenatally detected HN and who had normal ultrasound scan in postnatal period were followed for 2 years without any prophylactic treatment with antibiotics . The result was satisfactory as they did not have any worsening of hydronephrosis or urinary tract infectionduring the follow up period (38).Mild variants with APD diameter <10 mm on antenatal scans were transient and resolved spontaneously on subsequent followup scans. In a systemic analysis on 25 studies (9), they demonstrated that isolated antenatal detected hydronephrosisresolved in 98% of the patients with APD less than 12 mm, but only 51 % was resolved for those who had larger APD.

In a study by sidhu et al , they noticed that despite various classification methods was used, babies who had renal pelvic diameter less than 12 mm mostly normalised and they mostly didn't have any problems. Since the measurement of renal pelvis in USG scan is always observer dependent , the severe hydronephrosis with APD more than 12 mm have a variable outcome (9).

In our study 60% of antenatally detected CAKUT resolved spontaneously at birth. In 2 other studies by Elder JS and Koff SA, it was reported that antenatally detected dilatation was transient and resolved spontaneously in more than 50% of cases.27-28 Severe forms of hydronephrosis (APD>12 mm) persisted on postnatal scans. In our study among the persisted hydronephrosis majority were more than 10 mm APD. Majority of the hydronephrosis below 8mm resolved spontaneously.

Cases with hydroureteronephrosis received antibiotic prophylaxis (29). Antibiotic prophylaxis was discontinued at 3 months for patients, if VCUG was normal and no further UTIs occurred (5). In study by Gokce et al , the most commonly detected underlying abnormalities were ureteropelvic junction obstruction (44.8 %), vesicoureteral reflux (30.0 %) and megaureter (9.5 %) in patients with postnatal hydronephrosis.

In study by Feldman DM et al, they found that in their study population 88 % of fetuses was diagnosed to have mild hydronephrosis .they noticed that most of them gets normalised in due course. They found 40 babies to have persisting problems with moderate and severe type of hydronephrosis. In that 40 cases they found 15 % of them normalised , 25 % of them improved findings , 48 % had the same findings and the rest 12 % had worsening of the findings during pregnancy. None of the babies in the severe group had normalisation of the findings. There were no cases of in utero resolution in the severe group (39).

In a study done in Iran by SadeghiBojd et al,200 patients with post natal hydronephrosis were screened. There was male preponderance. Of them who underwent first postnatal control USG , 65% had normal, 18% mild/moderate and 17% severe hydronephrosis. 167 patients had VCUG of whom 20.82% with VUR. DTPA done for 112 patients with following resultsof whom, 50 patients had obstruction and 62 patients showed no obstructive finding. The final results were 54% of 200 patients recovered by conservative therapy, 12.5% by surgery and remaining improved without any surgical intervention.

In study done by Sairam S et al reported that fetalhydronephrosis was identified in 268 out of 11,465 mothers(2.3%) . Out of 268 caes , 216 were found to havemild hydronephrosis (80.6%), whereas the remaining were moderate or severe hydronephrosis(52 cases out of 268, i.e, 19.4%) . 88 % of the cases had resolution of hydronephrosis in the antenatal itself or during the early neonatal period. No intervention was needed in the mild hydronephrosis group. Surgery was needed in post natal period for one third of the babies who had either moderate hydronephrosisor severe hydronephrosis.Surgery was required in only1 in 1000 births in their study population required surgery.

In our study total 86 out of 108 was normalized in our study (79.6%) in the follow up period of upto 6 months. During the follow up period infants did not have any urinary tract problems. Issues for infections, hypertension , weight gain were all noted. Micturatingcystourethrogram is done for patients who had unilateral / bilateral hydronephrosis having renal pelvic AP diameter more than

10 mm, grade 3-4 SFU and with ureterohydronephrosis**.**In the follow up period subsequently 12 was normalised in PN scan 2 and 9 in PN scan 34 were lost follow up (3.7% of the study population) during the study period. 6 babies had surgery . 4 MCDK and 1 Medullary nephrocalcinosis ,one unilateral bulky kidney was a variant in study .other 6 were in follow up . Their follow up status had no issues of renal problems and thriving well. 6 babies had surgery of which 4 had pyeloplasty and 2 had cystoscopy with fulgration.

1 baby with MCDK on follow up DMSA was done with smaller left kidney with significant parenchymal dysfunction . LK – 5 % ; RK – 95%. 1 baby with medullary nephrocalcinosis, have good renal function on follow up and baby is thriving well.

LIMITATIONS OF THE STUDY

- Since the antenatal ultrasound was done by different obstetricians and not the same person, inter observer variation is a major limitation in the study.

- Being a tertiary care center, a significant proportion of cases are referred patients. The high prevalence of CAKUT is most probably due to this reason. This study therefore does not reflect the actual prevalence in the community, which may be much lower..

CONCLUSION

1. The prevalence ofCAKUT in antenatal scans is 4.2%, while in postnatal it is only 1.65%.

2. Only 50% of antenatally diagnosed CAKUT is detected in the 2nd trimester scan. Approximately one third of them, mainly unilateral hydronephrosis normalises in the 3rd trimester scan

3. 50% of unilateral hydronephrosis detected in 2nd trimester scan normalised in 3rd trimester scan, compared to only 6 out of 23 bilateral hydronephrosis(26%).

4. Hydronephrosis is the commonest anomaly picked up in third trimester scan- 58% were unilateral hydronephrosis and 33% were bilateral hydronephrosis.

5. Antenatally diagnosedCAKUT in 65 of the 108 babies (60%) has normalised in the first postnatal scan, while an additional 12 (11%) has normalised in 2nd postnatal scan and 9 (8%) normalised 3rd postnatal scan. Overall 86 of 108 (79%) have normalised by 4 to 6 months.

6. 34 of 51 unilateral hydronephrosis (67%) was detected in the 3rd trimester, normalised in the first postnatal scan compared to 13 of 29(45%) bilateral hydronephrosis normalised in first postnatal scan.

7. Among babies with abnormal first postnatal scan 2 of 20 babies with unilateral hydronephrosis(10%) , 2 of 11 bilateral hydronephrosis(18%) and 2 of 3 with hydroureteronephrosis(66%) required surgery in first 6 months.

8. Overall 6 of 108 babies with antenatally diagnosed CAKUT had medical renal disease (4 with multicystic dysplastic kidney , 1 with medullary nephrocalcinosisand 1 with unexplained bulky kidney), while 6 babies required surgery (4 had Pyeloplasty for hydronephrosis and 2 had Cystoscopy with fulgration for PUV) and 6 babies(4 with unilateral hydronephrosis and 2 with bilateral hydronephrosis) are on medical follow up.

ARPKD – infantile type , cystic kidney disease, renal hypoplasia and dysplasia of medulla are the other causes of renal failure in neonates with potter syndrome. The babies born with absence of both kidneys will die of pulmonary failure due to hypoplasia of lungs rather than renal failure(4).

Figure 4. USG of fetal abdomen shows that both the renal fossae are not occupied by kidneys, and are occupied by the adrenal glands producing low lying adrenal sign.

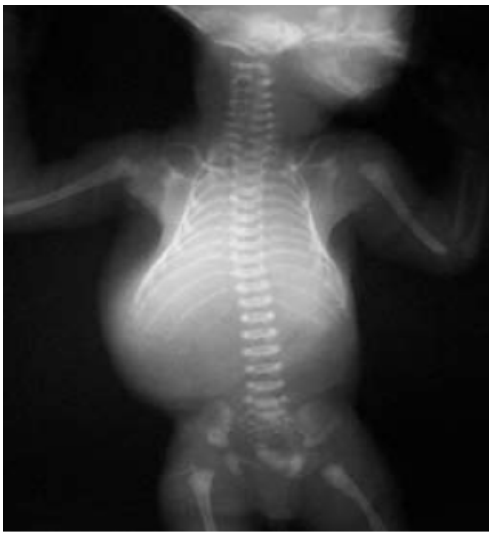


Fig 5: CXR showing bell-shaped thorax, suggestive of pulmonary hypoplasia

Fig 6: Potter facies

Ectopic kidney :

The prevalence of ectopic kidneys is about 1 in 1000 pregnancies. During renal embryogenesis it normally ascends from the pelvis into lumbar region. Renal ectopia occurs when the process of ascending from sacral to lumbar region is incomplete. Ectopic kidneyis seen in pelvis , iliac region, thoracic region and contralateral position. The kidneys get fused when the ectopia is bilateral. Fusion is more common in lower pole resulting in horseshoe kidney. Horseshoe kineys is more prevalent in turner syndrome. The incidence of wilms tumour in children with horse shoe kidney is four times more than other children.

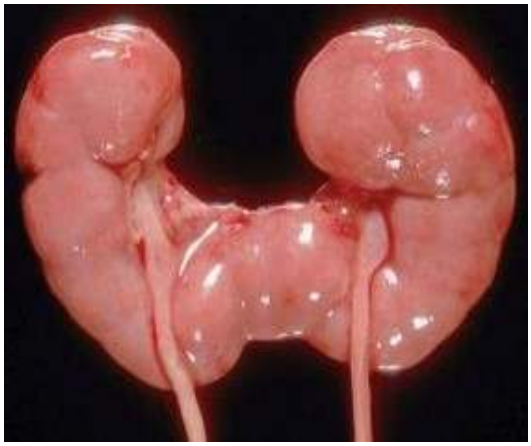


Fig 7 : Horse shoe kidney - both fused in the lower pole

Multicystic dysplastic kidney (MCDK):

The developmental malformation of kidney that affect its size, shape or structure is referred as renal dysgenesis. There are three types of dysgenesis : dysplastic , hypoplastic and cystic. Hypoplasia means there is decrease in

number of nephrons, it can occur as isolated condition. The term dysplasia denotes focal , diffuse or segmentally arranged primitive structures resulting in abnormal metanephric differentiation. Other elements apart from renal tissues like cartilages can be seen. MCDK can involve the entire kidney or only a certain part. In a kidney when cysts are developed, it is known as cystic dysplasia**. W**hen the entire kidney is dysplastic with predominance of cysts, it is known asmulticystic dysplastic kidney (4).

The etiology of MCDK is still unclear. Some causes considered are infections, teratogenicdrugs , genetic disturbances and urinary tract obstructions. Mutations in the EYA1, SIX1, and PAX2 genes have been correlated. In a family PAX2 mutation had MCDK(as well as other renal anomalies) affected members that has occurred across three generations. Certain antiepileptic medications, infections such as theenterovirus, cytomegalovirus, and adenovirus have also been considered as contributing factors (18).

Fig 8 : Multicystic dysplastic Kidney (MCDK)

Fig 9 : USG of a MCDK patient

The USG of a Multicystic dysplastic kidney shows multiple cysts , giving a appearance of "bunch of grapes". The DTPA renal scan shows no renal function.In patients with MCDK conservative management approach is routinely practiced in many centres. One reason is, this condition is detected antenatal ultrasound and it can be followed up in the post natal period. Many researchers have found that multicysticdysplastic kidney regress over the time. In a study reserachers have noted complete involution rates vary from 19–74% over 9 months to 10 years. Surgical approach is needed when patients have complications such as urinary tract infections, bleeding , flank pain , hypertension and malignant transformation. In studies done by Nishio et al , they found that ultrasound results of MCDK doesn't necessarily mean the involution has completely occurred. USG cannot detect small remnants from an involute cyst.

In unilateral MCDK , the contralateral kidneys are commonly affected. To evaluvate the kidney function , DMSA and VCUG are usually done. A dimercaptosuccinic acid scan (DMSA) is a nuclear medicine scan that generates tomographic and three-dimensional pictures of the kidneys. It detects the cortical scarring caused by contralateral abnormalities and how the kidneys are functioning. It can be used to distinguish between upper and lower UTI. But DMSA scans are not useful in differentiating contralateral renal abnormalities.

Vesicoureteral reflux causes urine to flow backwards from the bladder into the ureter or even the kidney. It causes pain and also scar the kidney or quite possibly disrupt the function of the kidney . A VCUG is a fluoroscopy exam that determines how the bladder is filled and if reflux occurs (18,19).

The abnormalities that affect the contralateral healthy kidney in MCDK are:

- Vesicoureteral reflux
- UVJ obstruction
- Hydronephrosis
- Ureterocele
- Crossed ectopia
- Echogenic kidney
- PUJ Obstruction

Polycystic kidney disease:

It is an autosomal inherited disorder. It is of two types,autosomal recessive (ARPKD) and autosomal dominant (ADPKD). Both the kidneys are involved. ADPKD is characterized by renal cyst development progressing &cyst enlargement with many extra renal manifestations. ADPKD is caused by mutation in PKD1 and PKD2 genes. PKD1 is located on the chromosome (short arm16p). PKD2 is located on the chromosome 4 (long arm 4q). TheADPKD is diagnosed when both the kidneys are enlarged with large cysts and the affected patient have an history of affected individual in the 1st-degree relative. Multiple hepatic lesions have been associated with it. The ARPKD manifests with mass in the abdomen palpated on both side of flanks during the neonatal or infancy period. There is history of oligohydraminos in antenatal period, respiratory distress at birth due to pulmonary hypoplasia, and history of spontaneous pneumothorax in the newborn period.Mutations in PKHD1 causes ARPKD. There will be no family history of renal cysts in child with ARPKD.Hypertension can develop in a child with this disease. Treatment is mainly supportive for both the conditions. Some experts included this polycystic kidney disease into the CAKUT spectrum. But the approach for this disease and management varies from the CAKUT. But most of the clinical features are not shared by common CAKUT conditions . These patients need a regular treatment and follow up (4,12).

Medullary Nephrocalcinosis :

Nephrocalcinosis is defined as renal calcification, is usually associated with hypercalciuric state. 7–64% of preterm neonates with gestational age less than 32 weeks or birth weight less than 1.5 kg , NC was diagnosed . Etiology of nephrocalcinosisin preterm is due to multiple factors. They include prematurity, LBW babies, severe respiratory disease and in imbalance between the stone-promoting factors & stone inhibiting factors.

Etiology :Nephrocalcinosis in preterm:

- Hypercalciuria
- High intake of calcium
- Low phosphorus
- Total Parenteral nutrition
- Diuretics - frusemide,
- Vitamin D
- Glucocorticosteroid
- Hyperoxaluria
- Fat malabsorption,
- Others :
    - Male, family history of kidney stones
    - Nephrotoxic medication, eg, Gentamicin.

The diagnosis is made by ultrasound examination. Spontaneous resolution of nephrocalcinosis occurs in 85 % of children by one year of age. (45). Prematurity itself can be associated with elevated B.P., comparatively smaller kidneys, and tubular dysfunctionin distal tubules. Added to it, nephrocalcinosis in preterm neonates can have long-term problems in renal function.The blood pressure andfunctionof kidneys should be followed up regularly for long term in prematurely born children with neonatalnephrocalcinosis.

Obstructive uropathy:

The urinary tract obstruction at the the junction ureteropelvic junction is the commonest cause of uropathy in babies (20).The incidence is one in 1500 births. Renal pelvis dilation will be seen in the ultrasound investigation done for PUJO. The ureter will not be dilated. The ureter will be involved in conditions like megaureter and UVJO. The ultrasound findings does not correlate clinically. The most of the dilatation gets resolved after birth. The fuctional scan is used for those with persisting anomalies. It is taken prior to surgery to take a decision. DTPA or MAG-3 are used. Ransley at al , concluded in his study that infants having renal pelvis APD greater than 20 mm are at increased risk of functional compromise of the kidney. MRI urogram is available now, it tells about the anatomy and the function of the kidneys The indications for surgery include <40% differential function of the hydronephrotic kidney on MAG3 scanning, a >20-mm anterior-posterior

diameter of the renal pelvis, pain, and infection. Pyeloplasty is the gold-standard treatment (20). The ultimate goal of the treatment in PUJO is to improve the renal drainage, maintain the kidney function or improving it and relieving from symptoms.

Posterior uretheral valve (21, 22) **:**

Posterior uretheral valve is also known as congenital obstructing posterior uretheral valve. The m.c.congenital obstructive lesion of urethra is PUV, occurring only in male infants and is associated with morbidities, including urinary tract infection, chronic renal failure, urinary incontinence and even death. Urethral valves arisesfrom the tissues of wolffian duct origin. PUV occurs early in gestation around 5-7 weeks.The incidence is about 1 in 10000-25000 live births (22). The clinical symptoms depends on severity of the obstruction caused by PUV. The fetus will be S.G.A and in USG scan will revealoligohydraminos.

There are 3 types of PUV. Type 1 is the most common type.

Type 1 - Valves representing folds extending inferiorly from the verumontanum to the membranous urethra.

Type 2 - Valves as leaflets radiating from the verumontanum proximally to the bladder neck, and

Type3 - Valves as concentric diaphragms within the prostatic urethra, either above or below the verumontanum.

Radiographic images of PUV :

- In antenatal USG , PUV is considered if there is
  - Marked distention and hypertrophy of the bladder.
  - Hydronephrosis and hydroureter (may or may not be present)
  - Severe oligohydraminos
  - Increased echogenicity of the kidneys
  - Key hole sign due to the distension of both the bladder and the urethra immediately proximal to the valve.

The USG findings are generally not seen before 26 weeks of gestation.

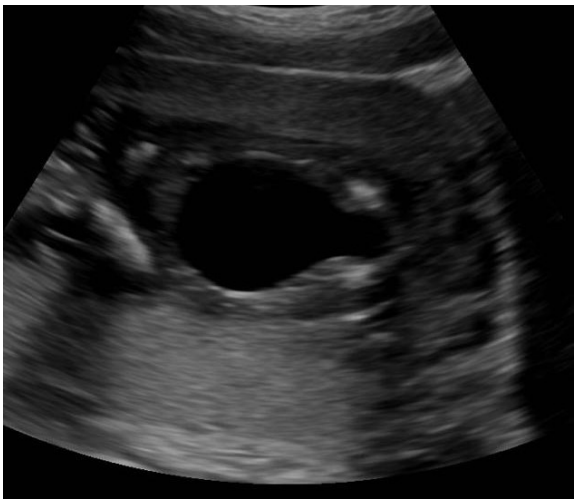


Fig 9 : USG showing keyhole sign

In postnatal scan, the findings are

- Key hole sign - bladder is typically thick-walled and trabeculated with an elongated and dilated posterior urethra.
- Hydronephrosis. In up to 10% of cases kidneys appear normal.
- Hyperechoic kidneys with loss of the normal corticomedullary differentiation.
- Posterior urethra examination ideally performed during micturition. Diameter of more than 6 mm is considered abnormal and is highly specific and sensitive to the diagnosis.
- Valve may be seen as an echogenic line.

In PUV due to the obstruction to urine flow is present , in some patients while voiding high tension is created within the bladder and it may lead to rupture and leads to accumulation of urine in other places.. It includes (1) Calyceal fornix rupture resulting in pararenalurinomas (2) Rupture of bladder intra-peritoneally(accumulated as intraperitoneal fluid, difficult to distinguish in ultrasound from ascites).

VCUGis the imaging of choice for diagnosing the posterior urethral valves. Images taken in the micturition phase gives the better confirmation.

VCUG findings include :

- Dilatation and elongation of the posterior urethra.
- Linear radiolucent band corresponding to the valve
- Vesicoureteric reflux seen in 50% of patients
- Bladder trabeculation or trabecula.

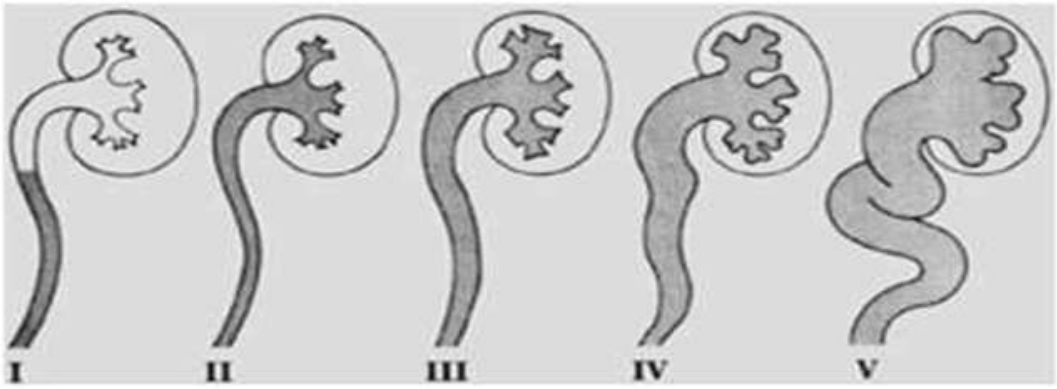
The overall prognosis depends on the degree and duration of obstruction. Antenatal treatment is by doing vesicoamniotic shunting. It allows urine to exit the bladder by the shuntcreated and obstruction to urethra is relieved. This procedure is done by ultrasound guidance and performed in expert hands. After birth the definitive treatment is surgery transurethral ablation (fulgration) of the offending valve.

Vesicoureteralreflux :

The most common uropathy in childhood is VUR (vesicoureteral reflux). It means the retrogradeflow of urine tothe ureter and kidney (upper urinary tract) at rest or while voiding. Primary VUR can either be due to position abnormality in ureterovesical junction (UVJ) or in its integrity. The prevalence of the Vesicoureteral reflux in children is not exactly known, as many of the children are asymptomatic. The prevalence of VUR in children with UTI is 30 % , in infants with posterior uretheral values is 60 % . it is estimated to be 0.4 – 1.8% in normal children.(23)

Classification of Vesicoureteral Reflux

TYPE	CAUSE
Primary	Congenital incompetence of the valvular mechanism of the vesicoureteral junction
Primary associated with other malformations of the ureterovesical junction	Ureteral duplication
	Ureterocele with duplication
	Ureteral ectopia
	Paraureteral diverticula
Secondary to increased intravesical pressure	Neuropathic bladder
	Non-neuropathic bladder dysfunction
	Bladder outlet obstruction
Secondary to inflammatory processes	Severe bacterial cystitis
	Foreign bodies
	Vesical calculi
	Clinical cystitis
Secondary to surgical procedures involving the ureterovesical junction	Surgery



International classification of VUR: (23, 24)

Grading of vesicoureteral reflux (23,24):

- Grade I: reflux into a nondilated ureter.
- Grade II: reflux into the upper collecting system without dilatation.
- Grade III: reflux into dilated ureter and/or blunting of calyceal fornices.
- Grade IV: reflux into a grossly dilated ureter.
- Grade V: massive reflux, with significant ureteral dilatation and tortuosity and loss of the papillary impression

The ureter is attached to the bladder in an oblique direction between the detrusor muscle and bladder mucosa. Reflux is prevented by the flap-valve mechanism created between them. VUR in children results in significant pyelonephritis. The inflammatory reaction caused by a pyelonephritic infection may lead to kidney injury or renal scarring. It is also known as reflux

nephropathy. VUR can occur as an isolated anomaly or it can occur secondary to other renal pathology. The pathogenic organisms ascend backwards and can result in renal scarring and injury.

The investigation of choice for detecting VUR is Voiding cystourethrography. The urinary catheter is placed and contrast is instilled into the urinary bladder by gravity dependent position. The contrast solution is kept at room temperature. When cold liquid is infused it will initiate an increased detrusor tone in young children and subsequently causes the bladder to empty at smaller volumes than warm liquids. Contrast medium should be instilled via the gravity drip method and never by hand injection. This prevents transmucosal contrast medium absorption and contrast reactions. Sudden push of contrast solution will cause a sudden rise of bladder pressure, which stimulates an unwanted premature bladder contraction at low volume. This could lead to underestimate any pathology and will result in inconclusive findings. Feeding tube is preferred for catheterisation instead of Foley catheter, since it has a smaller lumen relative to its outer diameter and is not suitable for VCUG. 5-F size feeding tube is appropriate for children under 1 year. Procedure should be explained to the parents as it create anxiety to them. Catheterization should be done by experienced personnel under strict aseptic precautions. The catheter should not be advanced any further than 1-2 cm after urine is collected. Now images are taken by serial radiographs by making the

child to void. After treating the active urinary infection and resolution of clinical symptoms , VCUG should be performed.

Indications for surgery :

- High grade reflux of type 4-5,
- When there is low chance of spontaneous resolution of symptoms,
- Scarring of the kidney,
- Recurrent urinary tract infections,
- Getting fever because of UTI, while on antibiotics continuous prophylaxis.
- Parental decision for surgery.

FDA approved the drug Deflux, a bulking agentfor the treatment of VUR from grades 1-4. 2010 guidelines of American urology association was revised for the patients having breakthrough febrile urinary tract infection to include endoscopy treatment.

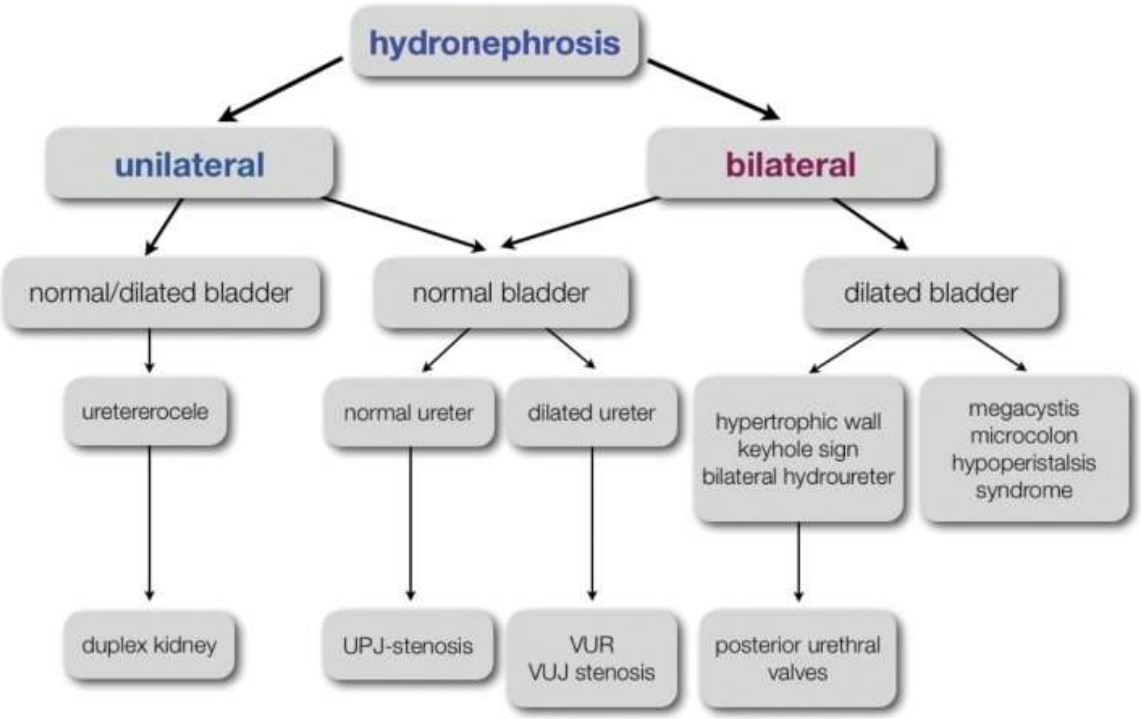
In a study by shaikh et al (26), mentioned that in systemic review of 33 studies for finding 99mtechnetiumdimercaptosuccinic acid (DMSA) scan abnormalities in children having urinary tract infection. They found that DMSA scan showing abnormalities in 57% of the children taken during acute

phase . Their features are consistent with findings of acute pyelonephritis.During follow up , scan 15% of the children had renal scarring.

Cooper et al mentioned in his study that the primary aim of surgical management is to prevent the febrile urinary tract infection and from pyelonephritis. But it is not yet proved that performing surgery will reduce the renal injury. Surgery will be benefitted in patients, having recurrent pyelonephritis and persistent reflux despite of conservative management. (27).

Evaluvation of antenatally detected CAKUT :

The hydronephrosis is the most commonly detected anomaly in the antenatal ultrasonography. The diverse etiology of fetalhydronephrosis is outlined as below.



Antenatal hydronephrosis is present whenthe foetal renal pelvis diameter is more than or equal to 4 mm during the 2nd trimester scan & more than or equal to 7 mm in 3rd trimester scan. It is classified into mild, moderate and severe based on renal pelvic APD size. The upper limit for a normal renal antero-posterior diameter in the third trimester is 7 mm. The AP diameter of more than or equal to 7 mm at 18 weeks (second trimester)denotes fetus with postnatal reflux or having obstruction. But those having same cut off at late gestation usually do not have significant pathology. There is always chance for inter observer variation and intra observer variation in measuring renal pelvic APD, since it is observer dependent. The renal pelvic AP diameter varies with gestational age, hydration status of mother and in bladder distension. (29).

In a study by Mallik M et al (34), concluded that the there is increasing sensitivity and accuracy of ultrasound screening at the time of 18–22 weeks. When APD of renal pelvis ≥4 mm , then the repeat scan at done after weeks of gestation. If the renal pelvis APD is ≥7 mm in the 2nd trimester then they should be referred to higher centre.

In study by sidhu et al (9), there is spontaneous resolution of antenatal hydronephrosis with renal pelvis APD less than 12 mm and SFU grade 1–2.

In study by lee at al (13), they found that the post natal renal anomaly is increased with the size of antenatal pelvic dilatation. Post natal renal anomaly persists in 11.9%patients with mild hydronephrosis, 45.1% of them with moderate hydronephrosisand 88.3% with severe hydronephrosis.

Classification of antenatal hydronephrosis based on renal pelvic anteroposterior diameter, APD (29)

Classification	Renal pelvic APD	
	Second trimester	Third trimester
Mild	4-6 mm	7-9 mm
Moderate	7-10 mm	10-15mm
Severe	>10mm	>15mm

In a study by Metzger et al (31), they concluded that severe hydronephrosis in postnatal scan has an positive correlation with the risk of urinary tract infection and surgery. There is negative correlation among those who had spontaneous resolutionofhydronephrosis in postnatal scan.

In study by Longpre et al (32), they reported that the risk of morbidity is low in those fetuseswho had minimal pelvic calyceal dilatation of 5-9mm. The morbidity is risk is more in the fetus having severe hydronephrosis with APD of more than 15mm, and these group need regular follow up.

In study by Sairam, Sasson et al ,88 % of them who were detected antenatally with mild hydronephrosis have resolution before birth or while